This document comprises a prospectus (the "**Prospectus**") relating to Acacia Pharma Group plc (the "**Company**" or "**Acacia Pharma**") prepared in accordance with the prospectus regulation rules (the "**Prospectus Regulation Rules**") of the UK Financial Conduct Authority (the "**FCA**") made pursuant to section 73A of the Financial Services and Markets Act 2000, as amended ("**FSMA**"). This Prospectus has been approved by the FCA as the competent authority under Regulation (EU) 2017/1129 (the "**Prospectus Regulation**") and has been filed with and made available to the public in accordance with Rule 3.2 of the Prospectus Regulation Rules. The FCA only approves this Prospectus as meeting the standards of completeness, comprehensibility and consistency imposed by the Prospectus Regulation. Such approval should not be considered as an endorsement of the Company or of the quality of the Ordinary Shares that are the subject of this Prospectus. Investors should make their own assessment as to the suitability of investing in the Ordinary Shares. In addition, this Prospectus has been drawn up as a simplified prospectus in accordance with Article 14 of the Prospectus Regulation. The Belgian Financial Services and Markets Authority ("**Belgian FSMA**") was notified of the passporting of this Prospectus in accordance with Article 25 of the Prospectus Regulation.

The Company and the Directors, whose names appear on page 39 of this document, accept responsibility for the information contained in this document. To the best of the knowledge of the Company and the Directors, the information contained in this document is in accordance with the facts and this document makes no omission likely to affect its import.

The Existing Ordinary Shares are admitted to trading on the regulated market of Euronext Brussels. Applications will be made for the New Ordinary Shares to be admitted to trading on the regulated market of Euronext Brussels ("**Admission**"). No application has been, or is currently intended to be, made for any of the New Ordinary Shares to be admitted to listing or trading on any other stock exchange.

Prospective investors should read the entire Prospectus and, in particular, Part II (*Risk Factors*) for a discussion of certain factors that should be considered in connection with an investment in the New Ordinary Shares. Prospective investors should be aware that an investment in the Company involves a degree of risk and that, if certain of the risks described in this Prospectus occur, investors may find their investment materially adversely affected. Accordingly, an investment in the New Ordinary Shares is only suitable for investors who are particularly knowledgeable in investment matters and who are able to bear the loss of the whole or part of their investment.

Acacia Pharma Group plc

(Incorporated under the Companies Act 2006 and registered in England and Wales with registered number 9759376)

Issue of 12,500,000 New Ordinary Shares

and

Admission of the New Ordinary Shares to trading on the regulated market of Euronext Brussels

Joint Global Coordinators and Joint Bookrunners

Jefferies **Guggenheim Securities**

Joint Bookrunner

Degroof Petercam

The New Ordinary Shares will, upon their Admission, rank equally in all respects with the Existing Ordinary Shares in issue prior to their Admission, including the right to receive all dividends or other distributions declared, made or paid on such Existing Ordinary Shares after their Admission. The New Ordinary Shares are not being made generally available to the public in conjunction with the Fundraising.

A copy of this document is available in English only and will from 14 August 2020 to 13 August 2021 (both days inclusive), be available for inspection at the addresses specified in Section 23 of Part XIV (*Additional Information*) of this document.

The date of this Prospectus is 14 August 2020.

NOTICE TO OVERSEAS INVESTORS

This Prospectus does not constitute an offer to sell, or the solicitation of an offer to buy or to subscribe for, Ordinary Shares to any person in any jurisdiction to whom or in which jurisdiction such offer or solicitation is unlawful and, in particular, is not for distribution in Australia, Canada (subject to limited exceptions described herein), Japan or South Africa. Neither the Company nor the Banks accept any legal responsibility for any violation by any person, whether or not a prospective investor, of any such restrictions. No action has been, or will be, taken in any jurisdiction that would permit a public offering of the New Ordinary Shares, or the possession, circulation or distribution of this Prospectus or any other material relating to the Company or the New Ordinary Shares, in any jurisdiction where action for that purpose is required.

The New Ordinary Shares have not been and will not be registered under the US Securities Act of 1933, as amended (the "**Securities Act**"), or with any securities regulatory authority of any state or other jurisdiction of the United States and may not be offered or sold, directly or indirectly, within the United States or to, or for the account or benefit of, US Persons (as defined in Regulation S (as defined below), except in transactions exempt from the registration requirements of the Securities Act and in accordance with any applicable securities laws of any state or other jurisdiction of the United States. Accordingly, the New Ordinary Shares are only being offered and sold (i) in the United States to persons reasonably believed to be "Qualified Institutional Buyers" as defined in Rule 144A ("**Rule 144A**") under the Securities Act ("**QIBs**") pursuant to an exemption from the registration requirements of the Securities Act and (ii) outside the United States in offshore transactions in reliance on Regulation S under the Securities Act ("**Regulation S**"). There will be no public offer of the New Ordinary Shares in the United States.

The New Ordinary Shares have not been approved or disapproved by the United States Securities and Exchange Commission (the "**SEC**"), any state securities commission in the United States or any United States regulatory authority, nor have any of the foregoing authorities passed upon or endorsed the merits of the offering of the New Ordinary Shares or the accuracy or completeness of this Prospectus. Any representation to the contrary is a criminal offence in the United States.

This Prospectus is being furnished by the Company in connection with an offering exempt from the registration requirements of the Securities Act, solely for the purpose of enabling a prospective investor to consider the acquisition of New Ordinary Shares described herein. The information contained in this Prospectus has been provided by the Company and other sources identified herein. This Prospectus is being furnished on a confidential basis only to persons in the United States reasonably believed to be QIBs and to other eligible persons outside of the United States. Any reproduction or distribution of this Prospectus, in whole or in part, in or into the United States and any disclosure of its contents or use of any information herein in the United States for any purpose, other than in considering an investment by the recipient in the New Ordinary Shares offered hereby in accordance with the offer and sale restrictions described herein, is prohibited. IN PARTICULAR, THIS PROSPECTUS MAY NOT BE FORWARDED TO ANY US PERSON OR US ADDRESS. Each prospective investor in the New Ordinary Shares, by accepting delivery of this Prospectus, agrees to the foregoing. The New Ordinary Shares are being offered in the United States to QIBs through the respective United States registered broker-dealer affiliates of the Banks. IF YOU HAVE GAINED ACCESS TO THIS TRANSMISSION CONTRARY TO ANY OF THE FOREGOING RESTRICTIONS, YOU ARE NOT AUTHORISED AND WILL NOT BE ABLE TO PURCHASE ANY OF THE SHARES DESCRIBED IN THE PROSPECTUS.

The offer, sale and/or issue of the New Ordinary Shares has not been, and will not be, qualified for sale or distribution under any applicable securities laws of Australia, Canada, Japan or South Africa. Subject to certain exceptions, the New Ordinary Shares may not be offered, sold or delivered within Australia, Canada, Japan or South Africa, or to, or for the benefit of, any national, resident or citizen of Australia, Canada, Japan or South Africa.

Persons who come into possession of this Prospectus should inform themselves about and observe any applicable restrictions and legal, exchange control or regulatory requirements in relation to the distribution of this Prospectus and the Fundraising. Any failure to comply with such restrictions or requirements may constitute a violation of the securities laws of any such jurisdiction.

Investors should rely only on the information contained in this Prospectus (and any supplementary prospectus produced to supplement the information contained in this Prospectus) when making a decision as to whether to purchase New Ordinary Shares. No person has been authorised to give any information or to make any representations other than those contained in this Prospectus in connection with the Fundraising and, if given or made, such information or representations must not be relied upon as having been authorised by or on behalf of the Company or the Directors or the Banks. Without prejudice to any

obligation of the Company to publish a supplementary prospectus pursuant to section 87G(1) of FSMA and Rule 3.4 of the Prospectus Regulation Rules, neither the delivery of this Prospectus nor any issue or sale made under this Prospectus shall, under any circumstances, create any implication that there has been no change in the business or affairs of the Company or of the Company and its subsidiaries taken as a whole since the date of this Prospectus or that the information contained herein is correct as at any time subsequent to the date of this Prospectus.

The contents of this Prospectus are not to be construed as legal, financial, business or tax advice. Each prospective investor should consult its own lawyer, financial adviser or tax adviser for legal, financial or tax advice in relation to the subscription or purchase of New Ordinary Shares. Prior to making any decision as to whether to invest in New Ordinary Shares, prospective investors should read this Prospectus in its entirety. In making an investment decision, a prospective investor must rely upon its own examination, analysis and enquiries of the Company and the terms of the Prospectus, including the merits and risks involved.

Jefferies International Limited ("**Jefferies**") and Guggenheim Securities, LLC ("**Guggenheim Securities**") have been appointed as joint global co-ordinators and joint bookrunners and Bank Degroof Petercam SA/NV ("**Degroof Petercam**") has been appointed as joint bookrunner and listing agent (Jefferies, Guggenheim Securities and Degroof Petercam together, the "**Banks**") in connection with Admission of the New Ordinary Shares and the Fundraising.

Jefferies is authorised and regulated by the FCA. Degroof Petercam is authorised by and under the supervision of the National Bank of Belgium and under the supervision on investor and consumer protection of the Belgian FSMA. Each of the Banks is acting exclusively for the Company and no one else in connection with the Fundraising and the contents of this Prospectus and will not regard any other person (whether or not a recipient of this Prospectus) as a client in relation to the Fundraising and will not be responsible to anyone other than the Company for providing the protections afforded to its clients nor for giving advice in relation to the Fundraising, the contents of this Prospectus or any transaction or arrangement referred to in this Prospectus.

Apart from the responsibilities and liabilities, if any, which may be imposed on the Banks by either the FCA, the National Bank of Belgium or the Belgian FSMA, or the regulatory regimes established thereunder, or under the regulatory regime of any jurisdiction where the exclusion of liability under the relevant regime would be illegal, void or unenforceable, none of the Banks or their respective affiliates accepts any responsibility whatsoever, and make no representation or warranty, express or implied, for the contents of this Prospectus, including its accuracy, completeness or for any other statement made or purported to be made by it or on behalf of it, the Company, the Directors or any other person, in connection with the Company, the New Ordinary Shares or the Fundraising and nothing in this Prospectus shall be relied upon as a promise or representation in this respect, whether as to the past or the future. Each of the Banks and their respective affiliates accordingly disclaims all and any liability whatsoever, whether arising in tort, contract or otherwise (save as referred to above), which it might otherwise have in respect of this Prospectus or any such statement.

In connection with the Fundraising, each of the Banks and their respective affiliates, acting as an investor for its or their own account(s), may acquire New Ordinary Shares, and in that capacity may retain, purchase, sell, offer to sell or otherwise deal for its or their own account(s) in New Ordinary Shares and other securities of the Company or related investments in connection with the Fundraising or otherwise. Accordingly, references in this Prospectus to the New Ordinary Shares being offered, acquired, placed or otherwise dealt in should be read as including any issue or offer to, or subscription, acquisition, dealing or placing by, the Banks and any of their respective affiliates acting as an investor for its or their own account(s). The Banks do not intend to disclose the extent of any such investment or transactions otherwise than in accordance with any legal or regulatory obligations to do so. In addition, in connection with the Fundraising, the Banks may enter into financing arrangements with investors, such as share swap arrangements or lending arrangements where New Ordinary Shares are used as collateral, which could result in the Banks acquiring shareholdings in the Company.

The Banks and their respective affiliates may have engaged in transactions with, and provided various investment banking, financial advisory and other services to, the Company for which they would have received customary fees. The Banks and their respective affiliates may provide such services to the Company and any of its affiliates in the future.

Recipients of this Prospectus are authorised to use it solely for the purpose of considering the acquisition of New Ordinary Shares and may not reproduce or distribute this Prospectus, in whole or in part, and may not

disclose any of the contents of this Prospectus or use any information herein for any purpose other than considering an investment in New Ordinary Shares. Such recipients of this Prospectus agree to the foregoing by accepting delivery of this Prospectus.

The New Ordinary Shares to be made available pursuant to the Fundraising will, on their Admission, rank equally in all respects with all other Ordinary Shares, including for all dividends and other distributions declared, made or paid on the New Ordinary Shares after their Admission.

INFORMATION TO DISTRIBUTORS

Solely for the purposes of the product governance requirements contained within: (a) EU Directive 2014/65/EU on markets in financial instruments, as amended ("**MiFID II**"); (b) Articles 9 and 10 of Commission Delegated Directive (EU) 2017/593 supplementing MiFID II; and (c) local implementing measures (together, the "**MiFID II Product Governance Requirements**"), and disclaiming all and any liability, whether arising in tort, contract or otherwise, which any "manufacturer" (for the purposes of the MiFID II Product Governance Requirements) may otherwise have with respect thereto, the New Ordinary Shares have been subject to a product approval process, which has determined that the New Ordinary Shares are: (i) compatible with an end target market of retail investors and investors who meet the criteria of professional clients and eligible counterparties, each as defined in MiFID II; and (ii) eligible for distribution through all distribution channels as are permitted by MiFID II (the "**Target Market Assessment**"). Notwithstanding the Target Market Assessment, distributors should note that: the price of the New Ordinary Shares may decline and investors could lose all or part of their investment; the New Ordinary Shares offer no guaranteed income and no capital protection; and an investment in the New Ordinary Shares is compatible only with investors who do not need a guaranteed income or capital protection, who (either alone or in conjunction with an appropriate financial or other adviser) are capable of evaluating the merits and risks of such an investment and who have sufficient resources to be able to bear any losses that may result therefrom. The Target Market Assessment is without prejudice to the requirements of any contractual, legal or regulatory selling restrictions in relation to the Fundraising. Furthermore, it is noted that, notwithstanding the Target Market Assessment, subject to certain limited exceptions, the Banks will only procure investors who meet the criteria of professional clients and eligible counterparties.

For the avoidance of doubt, the Target Market Assessment does not constitute: (a) an assessment of suitability or appropriateness for the purposes of MiFID II; or (b) a recommendation to any investor or group of investors to invest in, or purchase, or take any other action whatsoever with respect to the New Ordinary Shares.

Each distributor is responsible for undertaking its own target market assessment in respect of the New Ordinary Shares and determining appropriate distribution channels.

EXCHANGE RATE INFORMATION

The following table sets forth, for the periods indicated, certain information concerning the exchange rates between pounds sterling and US dollars. The exchange rates reflect the rates as reported by the US Federal Reserve Board.

	Noon Buying Rate			
	Period End	Average[(1)]	High	Low
	($ per £1.00)			
Period:				
2015	1.475	1.528	1.588	1.465
2016	1.234	1.356	1.480	1.216
2017	1.353	1.289	1.358	1.212
2018	1.276	1.336	1.433	1.252
2019	1.327	1.277	1.335	1.207
Month:				
January 2020	1.320	1.308	1.320	1.298
February 2020	1.278	1.295	1.305	1.278
March 2020	1.245	1.237	1.310	1.149
April 2020	1.260	1.242	1.262	1.223
May 2020	1.232	1.230	1.251	1.213
June 2020	1.237	1.252	1.276	1.228
July 2020	1.313	1.270	1.313	1.247

(1) The average of the noon buying rate for pounds sterling on the last day of each full month during the relevant year or each business day during the relevant month indicated.

The following table sets forth, for the periods indicated, certain information concerning the exchange rates between euros and US dollars. The exchange rates reflect the rates as reported by the US Federal Reserve Board.

	Period End	Average[(1)]	High	Low
	($ per €1.00)			
Period:				
2015	1.086	1.110	1.202	1.052
2016	1.055	1.107	1.152	1.038
2017	1.202	1.130	1.204	1.042
2018	1.146	1.182	1.249	1.128
2019	1.123	1.119	1.152	1.091
Month:				
January 2020	1.108	1.110	1.119	1.100
February 2020	1.100	1.091	1.106	1.079
March 2020	1.102	1.105	1.142	1.068
April 2020	1.093	1.087	1.097	1.080
May 2020	1.111	1.091	1.111	1.080
June 2020	1.124	1.126	1.139	1.112
July 2020	1.182	1.149	1.182	1.124

(1) The average of the noon buying rate for euros on the last day of each full month during the relevant year or each business day during the relevant month indicated.

With effect from 1 January 2019, the Company changed its presentational currency from pounds sterling to US dollars and the Group has presented its consolidated financial statements in US dollars since that time. Financial information presented in this Prospectus for the financial year ended 31 December 2018 remains in pounds sterling and is derived from the audited financial statements for the year ended 31 December 2018 incorporated by reference in this Prospectus. Unaudited financial information presented in this Prospectus for the financial year ended 31 December 2018 in US dollars is derived from the unaudited comparative presented in the financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus. For convenience and unless otherwise indicated, sterling amounts have been translated into US dollars using the procedures set forth below:

- Assets and liabilities were translated into US dollars at closing rates of exchange. Trading results were translated into US dollars at the rates of exchange prevailing at the dates of transaction or average rates where these are a suitable proxy. Differences resulting from the retranslation on the opening net assets and the results for the period have been taken to foreign currency translation reserve, a component within shareholders' equity.
- Share capital, share premiums and other reserves were translated at historic rates prevailing at the dates of transactions.
- All exchanges rates used were extracted from the Group's underlying financial records.

Foreign currency translation reserve was set to zero as of 1 January 2015, the transition date to IFRS. Cumulative currency translation adjustments are presented as if the Group had used US dollars as the presentation currency of its Group financial statements since that date.

The exchange rates used were as follows:

GBP / USD	**FY2018**	**HY2018**	**FY2017**	**FY2016**	**FY2015**	**FY2014**
Average rate	1.336056	1.381137	1.287513	1.350331	1.58022	—
Closing rate	1.273723	1.320829	1.349164	1.2341	1.48214	1.556723

These translations should not be considered representations that any such amounts have been, could have been or could be converted into US dollars at that or any other exchange rate as of that or any other date.

TABLE OF CONTENTS

PART I

SUMMARY

Introduction and warnings

Introduction

Acacia Pharma Group plc has its registered office at The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH (telephone number: 01223 919760). The Company's LEI code is 213800SLDKXWKT6E3381.

The securities which the Company intends to issue are ordinary shares of £0.02 each with ISIN GB00BYWF9Y76.

This document comprises a prospectus relating to the Company prepared in accordance with the Prospectus Regulation and the Prospectus Regulation Rules. A copy of this document has been filed with the FCA and approved on 14 August 2020. The address of the FCA is 12 Endeavour Square, London E20 1JN and its contact number is 0300 500 8082 from the UK, or +44 207 066 1000 from abroad.

Warnings

This summary should be read as an introduction to this Prospectus. Any decision to invest in the securities should be based on consideration of this Prospectus as a whole by the investor. The investor could lose all or part of their invested capital. Where a claim relating to the information contained in this Prospectus is brought before a court, the plaintiff investor might, under national law, have to bear the costs of translating this Prospectus before legal proceedings are initiated. Civil liability attaches only to those persons who have tabled the summary including any translation thereof, but only where the summary is misleading, inaccurate or inconsistent when read together with the other parts of this Prospectus, or where it does not provide, when read together with the other parts of this Prospectus, key information in order to aid investors when considering whether to invest in such securities.

Key information on the issuer

Who is the issuer of the securities?

The Company was incorporated and registered in England and Wales under the Companies Act as a private company limited by shares on 2 September 2015 under the name Cityviva Limited, with registered number 9759376. On 22 September 2015, the Company was registered as a public company limited by shares and changed its name to Acacia Pharma Group plc. On 19 December 2016, the Company was registered as a private company limited by shares and changed its name to Acacia Pharma Group Limited. On 21 February 2018, the Company was registered as a public company limited by shares and changed its name to Acacia Pharma Group plc. The Company is a holding company for Acacia Pharma Limited, a private company limited by shares incorporated in England and Wales (the "**Operating Company**") and Acacia Pharma, Inc, a corporation incorporated under the laws of Delaware (the "**US Subsidiary**").

The principal legislation under which the Company operates, and under which the New Ordinary Shares will be created, is the Companies Act and regulations made thereunder. The Company operates in conformity with its constitution.

The Company is a Euronext Brussels-listed hospital pharmaceutical group founded in 2007 and based in Cambridge, UK with US operations based in Indianapolis, Indiana. The Group is building a speciality US-based hospital sales and marketing organisation focused on the development and commercialisation of new treatments for surgical and cancer patients.

The Group has identified important and commercially attractive nausea and vomiting unmet needs and has developed two antiemetic products seeking to meet those needs, based on the same active ingredient, amisulpride, a dopamine antagonist. BARHEMSYS®, which was approved by the FDA on 26 February 2020, has been developed for the management of post-operative nausea and vomiting (PONV), including for (i) the rescue treatment of patients who suffer PONV despite having received prior prophylaxis with other antiemetics and (ii) the prophylaxis of PONV in combination with other antiemetics in higher risk patients. The anticipated main users of BARHEMSYS® will be anaesthesiologists and surgical doctors. In addition, APD403 is being developed by the Group for chemotherapy-induced nausea and vomiting (CINV), in particular for the management of delayed nausea in the two to five days following chemotherapy.

The Group has also acquired the licencing rights in the US to an additional product, BYFAVO™, which was approved by the FDA on 2 July 2020. BYFAVO™ is a rapid onset/offset sedative for use in

procedural sedation, which the Company expects could be promoted through the same sales channels as are targeted for BARHEMSYS®.

So far as is known to the Company, as at the date of this document, the following Shareholders held, directly or indirectly, three per cent or more of the Company's voting rights:

Shareholder	Number of Ordinary Shares	Percentage of voting rights (%)
Cosmo	17,500,140	24.05
Gilde	16,943,822	23.28
Lundbeckfond	12,468,955	17.13
F-Prime	3,692,446	5.07
Axa Investment Managers	2,650,846	3.64

Acacia Pharma has a management team which includes Mike Bolinder, the Chief Executive Officer, Gary Gemignani, the Chief Financial Officer and Dr Gabriel Fox, the Chief Medical Officer. Mike Bolinder is the sole Executive Director.

Mike Bolinder joined Acacia Pharma in August 2015 as Vice President of Marketing. Mike was promoted to Chief Commercial Officer in November 2017 and to Chief Executive Officer (when he was also appointed as a Director) on 1 August 2019. Mike has more than 17 years of experience in the pharmaceutical industry.

Gary Gemignani succeeded Christine Soden (who had served as Chief Financial Officer since July 2015) as Chief Financial Officer with effect from 1 March 2020. Gary's career in healthcare spans over three decades, including senior management/executive positions at several pharmaceutical and biopharmaceutical companies. Most recently, he served as chief financial officer of Synergy Pharmaceuticals, Inc.

Dr. Gabriel Fox has served in a variety of roles in clinical development, medical affairs and global marketing since joining the pharmaceutical industry in 1997. In his most recent position prior to joining Acacia Pharma in 2008, Gabriel was Head of Global Oncology Marketing at Roche.

The Company's statutory auditors are PricewaterhouseCoopers LLP.

What is the key financial information regarding the issuer?

The Company's consolidated key financial information is set out below.

Consolidated statement of comprehensive income

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Continuing operations:					
Research and development expenses	(3,766)	(5,031)	(3,928)	(2,511)	(623)
Sales and marketing expenses	(6,943)	(9,336)	(14,019)	(8,103)	(7,781)
Administrative expenses	(4,326)	(5,679)	(4,447)	(2,235)	(4,373)
Operating loss	**(15,035)**	**(20,046)**	**(22,394)**	**(12,849)**	**(12,777)**
Finance income	926	1,237	432	247	39
Finance expense	(2,069)	(2,764)	(1,545)	(896)	(2,523)
Loss before income tax	**(16,178)**	**(21,573)**	**(23,507)**	**(13,471)**	**(15.261)**
Taxation credit	660	881	668	352	65
Loss for the period	**(15,518)**	**(20,692)**	**(22,839)**	**(13,119)**	**(15,196)**
Exchange differences on translation of foreign operations	1,169	(2,023)	(78)	91	360
Total comprehensive expense for the period	**(14,349)**	**(22,715)**	**(22,917)**	**(13,028)**	**(14,836)**
Basic and diluted losses per Ordinary Share	(35)p	$(0.47)	$(0.43)	$(0.25)	$(0.24)

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

Consolidated statement of financial position

	31 December 2018 £'000 audited	31 December 2018 $'000 unaudited[1]	31 December 2019 $'000 audited	30 June 2020 $'000 unaudited
Assets				
Non-Current Assets				
Right-of-use asset	—	—	**372**	**325**
Intangibles	—	—	—	**11,180**
Total Non-Current Assets	—	—	**372**	**11,505**
Other receivables	312	397	609	221
Current income tax assets	686	874	679	700
Cash and cash equivalents	29,353	37,443	17,009	24,612
Total Current Assets	**30,351**	**38,714**	**18,297**	**25,533**
Total Assets	**30,351**	**38,714**	**18,669**	**37,038**
Equity and Liabilities				
Equity attributable to equity holders				
Share capital	1,067	1,581	1,619	1,954
Share premium	54,858	75,454	75,588	110,083
Profit and loss account	31,357	54,078	31,225	16,029
Share-based payments reserve	997	1,354	3,791	5,171
Merger reserve	(69,136)	(106,625)	(106,625)	(106,625)
Foreign currency translation reserve	—	(1,172)	(1,250)	(890)
Total Equity	**19,323**	**24,670**	**4,348**	**25,722**
Liabilities				
Non-current liabilities				
Loans and other borrowings	6,968	8,867	4,701	2,719
	6,968	**8,867**	**4,701**	**2,719**
Current liabilities				
Trade and other payables	3,726	4,727	4,167	3,184
Loans and other borrowings	334	450	5,453	5,413
	4,060	**5,177**	**9,620**	**8,597**
Total Liabilities	**11,028**	**14,044**	**14,321**	**11,316**
Total Equity and Liabilities	**30,351**	**38,714**	**18,669**	**37,038**

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented as of 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

Consolidated cash flow statement

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Cash flows from operating activities:					
Cash used in operations	(11,972)	(15,863)	(20,665)	(14,453)	(11,942)
Income tax credit received	323	432	834	—	
Net cash used in operating activities	**(11,649)**	**(15,431)**	**(19,831)**	**(14,453)**	**(11,942)**
Cash flows from investing activities:					
Interest received	**202**	**246**	**432**	**271**	**39**
Net cash generated from investing activities	**202**	**246**	**432**	**271**	**39**
Cash flows from financing activities:					
Proceeds of issuance of Ordinary Shares	—	49,379	180	—	22,339
Issue costs of Ordinary Shares	35,832	(2,296)	(8)	—	(255)
Repayments of lease liabilities – principal and interest	(1,652)	—	(101)	(56)	(58)
Loan proceeds	7,671	10,000	—	—	—
Costs of securing term loan	(494)	(644)	—	—	—
Loan repayments	(4,500)	(6,215)	—	—	(2,221)
Interest and fees paid on loans	(1,193)	(1,324)	(998)	(504)	(427)
Net cash generated / (used in) / from financing activities	**35,664**	**48,900**	**(927)**	**(560)**	**19,378**
Net increase / (decrease) in cash and cash equivalents	24,217	33,715	(20,326)	(14,742)	7,475
Cash and cash equivalents at beginning of the period	3,070	4,142	37,443	37,443	17,009
Effect of exchange rate movements on cash held	2,066	(414)	(108)	28	128
Cash and cash equivalents at end of the period	**29,353**	**37,443**	**17,009**	**22,729**	**24,612**

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

What are the key risks that are specific to the issuer?

The Group has incurred losses from inception and it is anticipated that the Group will incur further losses for the foreseeable future. No revenues have been generated from product sales to date, and the Group continues to incur significant development, commercialisation and other expenses related to its ongoing operations.

The Group will continue to seek to finance future requirements through debt or equity offerings. Additional capital may not be available on acceptable terms, or at all. Even if the Fundraising is successful, if additional capital is not available, the Group will be unable to commercialise BARHEMSYS® or BYFAVO™ beyond the fourth quarter of 2021. If a lack of available financing for future requirements means that the Group is unable to expand its operations or otherwise capitalise on its business opportunities, or if it must delay, limit, reduce or terminate: (i) clinical trials or other research and development activity; or (ii) the establishment of sales and marketing channels required to effectively commercialise its products, the Group's business, financial condition, results of operations and prospects could be materially adversely affected.

The widespread health crisis caused by COVID-19 has adversely affected the global economy. The future development of the outbreak is highly uncertain and there is no assurance that the outbreak will not have a material adverse impact on the future results of the Company. The extent of the impact will depend on the geographical range of the virus, infection rates, the severity and mortality rates of the virus, the timing and efficacy of a vaccine, the steps taken nationally and globally to prevent the spread of the virus, as well as fiscal and monetary stimuli offered by governments globally. If the negative impact from the COVID-19 pandemic continues, the Group's results may be worse than expected. Restricted access to healthcare settings and the postponement of medical conferences as a result of COVID-19 has already resulted in an adjustment to the Group's commercialisation strategies. Further, during the crisis in the US, the majority of hospitals

have postponed or cancelled all unnecessary and elective surgeries and continued reduction in such procedures in which the Company's products may be used may limit uptake and market acceptance. The full extent of the impact is currently unknown and will depend on future developments, such as the ultimate duration and the severity of the spread of COVID-19 in the US and globally, the effectiveness of federal, state, local and foreign governments' mitigation actions, together with the pandemic's impact on the US and global economies.

The commercial success of BARHEMSYS® and BYFAVO™ and any of the Group's future products will depend upon the acceptance of such products as safe and effective by the medical community and patients and the products' pharmoeconomic benefits. The market acceptance of the Group's products could be affected by a number of factors, such as cost-effectiveness, ability of the Company to obtain inclusion on the formulary of approved products within hospitals, success of existing products addressing the Group's target markets or the emergence of equivalent or superior products, and changes in standards of care, among others. In addition, market acceptance depends on the effectiveness of the Group's marketing strategy, and, to date, the Group has not engaged in sales or marketing. The rate and speed of acceptance will directly impact on the commercial success of each product and the Company's ability to generate revenues and become profitable.

The Group does not have a fully established sales and marketing infrastructure and has not been engaged in the sale or marketing of pharmaceutical products. To achieve commercial success for any approved product, the Group must complete the development of its sales and marketing organisation. The Group is currently establishing its own sales and marketing capabilities to promote BARHEMSYS® and BYFAVO™ in the US with a targeted sales force. There are risks and expense involved with establishing the Group's own sales and marketing capabilities and in entering into arrangements with third parties to perform these services. Even if the Group establishes sales and marketing capabilities, it may fail to launch or to market its products effectively given its limited experience in the sales and marketing of pharmaceutical products.

The Group's existing and expected future debt agreements require the Group to make debt service payments and restrict its business and operations, which diverts funding from commercialisation and research and developments efforts, and if the Group does not effectively manage its debt service and compliance with covenants, its financial conditions and results of operations could be adversely affected. In addition, the Group financed its milestone payment obligation to Cosmo on 27 July 2020 through a €15 million drawdown under the €25 million Loan Agreement from Cosmo, which will be repayable in 24 equal monthly instalments starting in July 2023 and which accrues interest daily, payable monthly, at the rate of 11 per cent per anum. The Group may finance its operations and future milestone payment obligations through further loans, increasing the Group's indebtedness, repayment obligations and reducing its cash resources which could otherwise be utilised to pursue its strategic objectives.

The Group has no experience of manufacturing its products on a commercial scale and is dependent on third party manufacturers for the manufacture and supply of the active pharmaceutical ingredient (API) and other components of all its products. The approval by the FDA of BARHEMSYS® was originally delayed due to pre-approval inspection issues identified at a third party manufacturer. Whilst those issues were resolved in order to obtain approval, any subsequent failure(s) by appointed third party manufacturers to comply with GMP could further delay or interrupt the manufacture of the Group's products and materially adversely affect its business.

It is difficult for a prospective investor to evaluate the Group's ability to commercialise products successfully and to assess the Group's future prospects. The Group's ability to generate future revenues and become profitable will depend upon its ability to successfully commercialise BARHEMSYS® and BYFAVO™, and subject to receipt of marketing authorisation, APD403. Any predictions about the Group's future success, performance or viability may not be as accurate as they might be if the Group had an established sales channel or established products on the market.

The Group's ability to compete and grow depends to a large extent upon the continued service of the current management team and the timely recruitment of the direct sales force. Members of the Group's management team may terminate their employment with the Group at any time subject to the terms of their employment contracts, which have notice periods of between zero (most US employees) to twelve months.

The Group will be subject to ongoing regulatory obligations and review by the FDA in particular and may still face future development and regulatory difficulties, which may result in additional expenses or the Group being subjected to sanctions or penalties for failure to comply with its regulatory obligations.

Potential product liability lawsuits against the Group could cause the Group to incur substantial liabilities and limit commercialisation of any products that the Group may develop and there can be no certainty that the Group can obtain adequate product liability insurance in order to protect it from potential claims.

Key information on the securities

What are the main features of the securities?

The type and class of securities being issued by the Company pursuant to the Fundraising are ordinary shares of £0.02 ("**Ordinary Shares**") and will be traded in Euros under the ticker symbol ACPH. The ISIN is GB00BYWF9Y76 and the Company's Legal Entity Identifier ("**LEI**") code is 213800SLDKXWKT6E3381. At the Latest Practicable Date, the issued share capital of the Company comprised 72,779,729 Ordinary Shares.

The Ordinary Shares (including the New Ordinary Shares to be issued by the Company pursuant to the Fundraising) rank *pari passu* as regards voting, entitlement to income and entitlement on a return of capital. There are no restrictions on the free transferability of the Ordinary Shares. In the event of insolvency, Shareholders will be entitled to a share in the capital of the Company in the same proportions as capital is attributable to them, only after the Company has settled all amounts owed to its creditors.

The Company has never declared or paid any cash dividends on its Ordinary Shares. The Company intends to retain future earnings, if any, to finance the operation of its business and does not anticipate paying any cash dividends in the foreseeable future. Any future determination related to the Company's dividend policy will be made at the discretion of the Board after considering the Group's financial condition, results of operations, capital requirements, business prospects and other factors the Board deems relevant, and subject to the restrictions contained in any future financing instruments.

Where will the securities be traded?

Application will be made for the New Ordinary Shares to be admitted to trading on the regulated market of Euronext Brussels. The New Ordinary Shares will be traded in Euros under trading symbol "ACPH" with ISIN code GB00BYWF9Y76. No application has been made for admission of the New Ordinary Shares to trading on any other stock exchange, and the Company does not currently intend to make any such application in the future.

It is expected that Admission of the New Ordinary Shares will become effective and that unconditional dealings in the New Ordinary Shares will commence on Euronext Brussels by no later than 8.00 a.m. CET on 18 August 2020.

What are the key risks that are specific to the securities?

Future sales and issuances of Ordinary Shares or rights to purchase Ordinary Shares, including pursuant to any equity incentive plans, could result in additional dilution of the percentage ownership of Shareholders and could cause the Ordinary Share price to fall. Following the issue of the New Ordinary Shares, Shareholders will suffer a dilution to their interests in the Company immediately prior to such event. Shareholders will be diluted by the issue of Ordinary Shares to Cosmo in consideration of a milestone payment of €5 million due upon the first commercial sale of BYFAVO™ by the Operating Company, which is expected to be satisfied by the issue of New Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the date of the first commercial sale of BYFAVO™ by the Operating Company.

The price of the Company's Ordinary Shares may be volatile, and all or part of an investment could be lost. The future trading price of the Company's Ordinary Shares may be subject to fluctuations in response to various factors, some of which are beyond the Group's control. In addition, the stock market in general and shares of life science companies in particular, have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

The Group does not anticipate paying any dividends in the foreseeable future and, therefore, investors will need to rely on capital appreciation, if any, for any return on their investment.

Key information on the offer of securities to the public and the admission to trading on a regulated market

Under which conditions and timetable can I invest this security?

There is no public offer of the New Ordinary Shares.

New Ordinary Shares are being made available under the Fundraising at the Placing Price.

The Fundraising is being made by way of subscriptions for the New Ordinary Shares by: (i) certain institutional and professional investors in the United Kingdom and Belgium and elsewhere outside the United States who are not US persons in reliance on Regulation S; and (ii) in the United States to persons reasonably believed to be QIBs.

The Fundraising is subject to satisfaction of conditions which are customary for transactions of this type as set out in the Placing Agreement, including, amongst others, Admission of the New Ordinary Shares occurring and becoming effective by no later than 8:00 a.m. CET on 18 August 2020 or such later time or date as the Company and the Banks may agree, and the Placing Agreement not having been terminated in accordance with its terms.

It is expected that Admission of the New Ordinary Shares will become effective and unconditional dealings in the New Ordinary Shares will commence on the regulated market of Euronext Brussels on 18 August 2020.

12,500,000 New Ordinary Shares will be issued to investors pursuant to the Fundraising. The New Ordinary Shares issued pursuant to the Fundraising will represent approximately 17.2 per cent of the Existing Ordinary Shares in issue prior to the Fundraising. Following the issue of the New Ordinary Shares to be allotted pursuant to the Fundraising, Shareholders will suffer dilution of approximately 14.7 per cent to their interests in the Company immediately prior to the Fundraising.

The total costs and expenses of, and incidental to, the Fundraising and Admission (including the admission fees, advisers' fees, professional fees and expenses and VAT thereon, if any) to be borne by the Company are estimated to be approximately €2.9 million. No commissions are payable by investors in respect of the Fundraising or Admission.

Why is this prospectus being produced?

The net proceeds payable to the Company from the Fundraising will be approximately €22.1 million (after deducting underwriting commissions and other offering-related fees and expenses plus VAT thereon, if applicable, of approximately €2.9 million).

The net proceeds of the Fundraising, together with the Group's existing cash resources and loan facilities, are expected to allow the Group to complete the establishment of its sales and marketing infrastructure, to launch BARHEMSYS® and BYFAVO™ to the hospital market in the US in late-2020 and to promote the products until the fourth quarter of 2021.

In accordance with the requirements of the Prospectus Regulation Rules, this prospectus is being produced in connection with the Company's application for the New Ordinary Shares to be admitted to trading on the regulated market of Euronext Brussels. There is no public offer of the New Ordinary Shares and the Fundraising is being underwritten, subject to the terms and conditions set out in the Placing Agreement. To the extent that any placee procured by the Banks fails to subscribe for any or all of the New Ordinary Shares allotted to it, the Banks shall themselves subscribe for such New Ordinary Shares at the Placing Price. In such circumstances, each Bank shall be required to subscribe for such New Ordinary Shares at the Placing Price only in respect of the placees it has procured.

There are no material conflicts of interest pertaining to the Fundraising or Admission.

PART II

RISK FACTORS

Any investment in the Ordinary Shares is subject to a number of risks. Prior to investing in the Ordinary Shares, prospective investors should carefully consider the factors and risks associated with any such investment in the Ordinary Shares, the Group's business and the industry in which it operates, together with all other information contained in this Prospectus, including, in particular, the risk factors described below. Prospective investors should note that the risks relating to the Group, its industry and the Ordinary Shares summarised in Part I (Summary) are the risks that the Directors believe to be the most essential to an assessment by a prospective investor of whether to consider an investment in the Ordinary Shares. However, as the risks which the Group faces relate to events and depend on circumstances that may or may not occur in the future, prospective investors should consider not only the information on the key risks summarised in Part I (Summary) but also, among other things, the risks and uncertainties described below.

The following is not an exhaustive list or explanation of all risks that prospective investors may face when making an investment in the Ordinary Shares and should be used as guidance only. Additional risks and uncertainties relating to the Group that are not currently known to the Group, or that the Group currently deems immaterial, may individually or cumulatively also have a material adverse effect on the Group's business, financial condition, results of operations and prospects and, if any such risk should materialise, the price of the Ordinary Shares may decline and investors could lose all or part of their investment.

An investment in the Ordinary Shares is suitable only for investors who are capable of evaluating the merits and risks of such an investment and who have sufficient resources to be able to bear losses (which may equal the whole amount invested) that may result from such an investment. An investment in the Ordinary Shares should constitute part of a diversified investment portfolio. If investors are in any doubt as to the consequences of their acquiring, holding or disposing of Ordinary Shares, or whether an investment in Ordinary Shares is suitable for them in the light of information in, or incorporated by reference into, this document or their personal circumstances, including the financial resources available to them, they should consult their stockbroker or other independent financial adviser authorised under FSMA or, in the case of investors outside the United Kingdom, another appropriately authorised independent financial adviser before making their own decision to invest in the Ordinary Shares.

RISKS RELATING TO THE GROUP'S FINANCIAL SITUATION

The Group has incurred losses from inception and it is anticipated that the Group will incur further losses for the foreseeable future.

The Company is a commercial stage biopharmaceutical company focused on developing and commercialising novel products to improve the care of patients undergoing serious medical treatments such as surgery, invasive procedures or chemotherapy. No revenues have been generated from product sales to date, and the Group continues to incur significant development, commercialisation and other expenses related to its ongoing operations. The Group reported net losses of $22.8 million and $20.7 million for the years ended 31 December 2019 and 31 December 2018 respectively, and $13.1 million and $15.2 million for the six months ended 30 June 2019 and 30 June 2020.

The Directors expect the Group to continue to incur losses for the foreseeable future and expect these losses to increase in connection with the launch of BARHEMSYS® and BYFAVO™. The Directors anticipate that the Group's expenses will increase as it commercialises BARHEMSYS® and BYFAVO™, including as a result of establishing sales, marketing and distribution infrastructure in the United States and making royalty payments to Paion UK Limited ("**Paion**"), which owns the licensing rights to BYFAVO™.

The Group may encounter challenges or delays in gaining market acceptance, which could adversely affect the Group's revenue, or encounter unforeseen expenses, difficulties, complications and delays in launching BARHEMSYS® or BYFAVO™. If BARHEMSYS® or BYFAVO™ fail to achieve market acceptance, the Group may never become profitable. Prior losses and expected future losses have had and will continue to have an adverse effect on Shareholders' equity. The size of future net losses will depend, in part, on the rate of future growth of expenses and the Group's ability to generate revenues. Even if profitability is achieved in the future, the Group may not be able to sustain profitability in subsequent periods.

The Group has never generated any revenue from BARHEMSYS® or BYFAVO™ and its ability to generate revenue from sales of its products and become profitable depends significantly on its success in a number of factors. The Directors cannot guarantee when, or if, the Group will attain profitability or positive cash flows.

The Group aims to begin selling BARHEMSYS® and BYFAVO™ in the second half of 2020. The commercial success of BARHEMSYS® and BYFAVO™ depends on a number of factors, including:

- maintaining regulatory approvals and marketing authorisation;
- the effectiveness of the sales, managed markets and marketing efforts by the Group;
- the Group's success in receiving hospital formulary approvals and achieving market acceptance;
- the occurrence of any side effects, adverse reactions or misuse, or any unfavourable publicity in these areas, associated with BARHEMSYS® or BYFAVO™; and
- the Group's ability to compete with existing products, including existing generic products, compared to which BARHEMSYS® or BYFAVO™ may be more expensive alternatives to currently available products which, in turn, may make it difficult for the Group to gain market share and, consequently, to achieve expected revenue levels.

The Group's revenues from the commercialisation of BARHEMSYS® or BYFAVO™ are subject to these factors, and may therefore be unpredictable and may fluctuate. The Group may never generate sufficient revenues from BARHEMSYS® or BYFAVO™ to reach or maintain profitability for the Company or to sustain its anticipated levels of operations. Moreover, the Group is obligated to make royalty payments to Paion pursuant to the BYFAVO™ Assignment Agreement based on net sales of BYFAVO™ and additional milestone payments to Cosmo pursuant to the BYFAVO™ Wind-Up Agreement that will be triggered upon accomplishing certain milestones in the net sales of BYFAVO™. Such royalty and milestone payments will impose additional costs as the result of sales of BYFAVO™ and will in turn reduce the net income realised as a result of revenues from sales of BYFAVO™. For additional information on these royalty and milestone payments, please refer to the description entitled "BYFAVO™ Acquisition" under Section 18 (*Material Contracts*) in Part XIV (*Additional Information*).

If additional capital required to fund the Group's operations is unavailable on reasonable terms, or at all, the Group may be unable to commercialise BARHEMSYS® or BYFAVO™ from the fourth quarter of 2021 onwards or complete the development of its other product candidates.

The Group has incurred substantial expenditures since inception and expects to continue to invest substantial amounts to launch and commercialise BARHEMSYS® and BYFAVO™ and to advance the clinical development of APD403. The Group's future funding requirements will depend on many factors, including, but not limited to:

- the amount of sales and other revenues the Group can generate, including the sales price and achieving hospital formulary approval;
- the cost of establishing and maintaining sales, marketing and distribution capabilities for any product candidate for which the Group may receive regulatory approval;
- the cost and timing of obtaining commercial-scale product supply;
- the outcome, timing and cost of regulatory approvals, the potential for the FDA or comparable regulatory authorities to require that more or different studies need to be performed than currently expected or that the application approval is not granted for each individual indication sought. In addition, any resubmission, amendment or failed applications to the FDA will incur additional costs and will result in delays in securing marketing approval and the availability of the Group's drugs to patients;
- the effect of competing technological and market developments and the time and cost to respond to them;
- the initiation, progress, timing, costs and results of clinical trials for the Group's product candidates, including the ability to enrol patients in a timely manner; and
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

Even if the Fundraising is successful, the Group will need to finance future requirements through new debt or equity offerings in order to commercialise BARHEMSYS® or BYFAVO™ from the fourth quarter of 2021 onwards and pursue the development of APD403. Additional capital may not be available on acceptable terms, or at all. If it were to raise additional funds through the issuance of additional equity securities that could result in dilution to Shareholders.

If a lack of available financing for future requirements means that the Group is unable to expand its operations or otherwise capitalise on its business opportunities, or if it must delay, limit, reduce or terminate: (i) clinical trials or other research and development activity; or (ii) the establishment of sales and marketing channels required to effectively commercialise its products, the Group's business, financial condition, results of operations and prospects could be materially adversely affected.

The incurrence of indebtedness could result in increased fixed payment obligations and the Group may be required to agree to certain restrictive covenants, such as limitations on its ability to incur additional debt, limitations on its ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact its ability to conduct its business. The Group could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and may be required to relinquish rights to some of its technologies or product candidates or otherwise agree to terms unfavourable to it, any of which may have a material adverse effect on its business, operating results and prospects. Further, any additional fundraising efforts may divert the Group's management from its day-to-day activities, which may adversely affect its ability to develop and commercialise its product candidates.

The Company's planned strategy to commercialise BARHEMSYS® and BYFAVO™ is dependent on completion of the Fundraising. In the unlikely event the Fundraising does not proceed to completion, the Group can continue as a going concern, but would need to obtain alternative debt or equity financing to commercialise BARHEMSYS® and BYFAVO™ as planned.

The 2020 Interim Financial Statements were prepared on the basis that the Group, in order to continue as a going concern, would not increase its cost base as planned (for the commercialisation of BARHEMSYS® or BYFAVO™) if the Group were unable to obtain debt or equity financing. The Fundraising, pursuant to which the Company has raised net proceeds of approximately €22.1 million, constitutes such an equity financing and the proceeds of the Fundraising allow the Group to proceed with its plans to commercialise BARHEMSYS®and BYFAVO™ while continuing as a going concern. However additional funding will be required in the fourth quarter of 2021. There is no guarantee that attempts to raise adequate additional financing on a timely basis will be successful and therefore this represents a material uncertainty, which may cast significant doubt about the Group's ability to continue as a going concern.

The Fundraising is being underwritten by the Banks, subject to the terms and conditions set out in the Placing Agreement, including Admission occurring no later than 18 August 2020 (or such later date as the Company and the Banks may agree). To the extent that any placee procured by the Banks fails to subscribe for any or all of the New Ordinary Shares allotted to it, the Banks shall themselves subscribe for such New Ordinary Shares at the Placing Price. In such circumstances, each Bank shall be required to subscribe for such New Ordinary Shares at the Placing Price only in respect of the placees it has procured.

In the unlikely event that the Fundraising does not proceed to completion and/or Admission does not occur as provided for in the Placing Agreement, the Directors believe that the Group can continue as a going concern, but the Group's plans to commercialise BARHEMSYS® or BYFAVO™ would be dependent on the Group obtaining alternative forms of financing. In those circumstances, the Directors consider that such alternative forms of financing following a scaled back launch of its products may be available to the Group in the form of additional debt facilities, receivables factoring and/or synthetic royalty type arrangements, albeit any such alternative financing arrangements would likely be on terms that would have a detrimental effect on the Group's expected financial position.

The Group's existing and expected future debt agreements require the Group to make debt service payments and restrict its business and operations, which diverts funding from commercialisation and research and development efforts, and if the Group does not effectively manage its debt service and compliance with covenants, its financial conditions and results of operations could be adversely affected. In addition, the Group has financed and may in the future finance its operations and milestone payment obligations through loans, increasing the Group's indebtedness, repayment obligations and reducing its cash resources which could otherwise be utilised to pursue its strategic objectives.

The Group has financed its business, and expects to finance its business in the future, in part with loan agreements entered into with its lenders and strategic partners. The Group is subject to limitations as the result of such agreements and is obligated to make debt service payments under such loan agreements that decrease its flexibility and impose additional costs. If the Group enters into further loan agreements or otherwise issues further debt, the continuing costs of debt service may reduce its cash resources and adversely affect the Group's ability to fund further development and commercialise its products.

As of 30 June 2020 the Group had net indebtedness of $8.13 million, which includes $7.8 million in secured debt outstanding from the $10 million in principal amount drawn in June 2018 under its loan and security agreement with Hercules Capital (the "**Hercules Facility**").

In addition, BYFAVO™ was approved by the FDA on 2 July 2020 and, pursuant to the terms of the BYFAVO™ Sub-Licence Agreement (as such terms survive pursuant to the BYFAVO™ Wind-Up Agreement), the Group owed Cosmo a milestone payment of €30 million, payable via the issue of Ordinary Shares of the Company in the amount €15 million (which was completed on 16 July 2020), plus €15 million in cash, which was paid on 27 July 2020, and financed through a drawdown on the unsecured loan provided by Cosmo to the Group (the "**€25 million Loan Agreement**", see Part XIV (*Additional Information*), Section 18.6 for a description thereof). This drawdown increased the Group net indebtedness to $25.2 million as of the date of this Prospectus.

As a result of the satisfaction of this milestone payment through debt financing, the Company will be subject to increased debt service obligations, including payment of principal and accrued interest, reducing its cash resources which could otherwise be utilised to pursue its strategic objectives and to commercialise its products. The principal drawn under the €25 million Loan Agreement will be repayable in 24 equal monthly instalments commencing in July 2023. The interest at the rate of 11 per cent (or 9 per cent following grant of certain security), shall accrue daily from the date of drawdown, and be payable monthly. The Group has agreed to pay all costs, fees and expenses relating to amendments or extensions of the loan and is required to pay certain taxes in connection with the €25 million Loan Agreement.

The agreements governing the Hercules Facility and the €25 million Loan Agreement impose, and similar debt finance agreements that the Group may enter into in the future may impose, various covenants which are customary for agreements of this nature that limit the Group's ability to, among other things:

- incur indebtedness without prior consent, subject to certain limited exceptions, such as those relating to the Group's ordinary course of business;
- provide security for other indebtedness, subject to similar customary exceptions; and
- dispose of assets or intellectual property, or parts thereof, without prior consent (which, in the case of the €25 million Loan Agreement, may include obtaining Cosmo's prior consent to sub-licensing of the Group's products).

If the Group is unable to successfully manage the limitations and decreased flexibility on its business due to its debt obligations, the Group may not be able to capitalise on strategic opportunities or grow its business.

The Group is, and expects to continue to be, exposed to foreign currency exchange risk.

The Group's consolidated financial statements are presented in US dollars but the Ordinary Shares are traded in Euros. Given the Group's intention to commercialise its product candidates principally in the US, the Directors believe the majority of the Group's sales and marketing costs will arise in the US and be incurred in US dollars, and the majority of its revenues will arise in the US and will be generated in US dollars. The Group's main discovery and development operational costs and its senior management costs are expected to be priced in a combination of pounds sterling, Euros and US dollars. As a result, the Group is exposed to both translational and transactional foreign currency exchange risk.

Translational foreign currency exchange risk arises when translating the value of the Company's non-UK assets and liabilities and the results of any non-UK subsidiaries into sterling. To the extent that there are fluctuations in exchange rates in these currencies, this would have an impact on the Company's accounts. The Group has presented its financial information in US dollars since publication of its financial information for the year ended 31 December 2019 and intends to continue to do so henceforward in order to reduce translational currency exposure. Transactional foreign currency exchange risk arises as a result of payments the Company makes or receives in local currencies and as a result of differences in exchange rates on the dates commercial transactions are entered into and the dates they are settled.

The Group intends to put in place hedging strategies to mitigate expected exchange rate impacts. However, no such measures are currently in place and there can be no certainty that the Group will be able to obtain sufficient exchange rate instruments, such as hedging products, forward exchange contracts or options to mitigate any adverse impact of exchange rate fluctuations, which could adversely affect the Group's financial condition and results of operations.

RISKS RELATING TO THE GROUP'S DEPENDENCE ON THIRD PARTIES

The Group has no experience manufacturing its products on a commercial scale and is dependent on third party manufacturers to manufacture and supply the API and other components for all its products. Problems with third party manufacturers could further delay or interrupt the Group's commercialisation plans and materially adversely affect its business.

The Group does not own or operate facilities for the manufacture of its products and there are currently no plans within the Group to build clinical or commercial scale manufacturing capabilities, given the availability of a number of suitable third party manufacturers and suppliers of the key active ingredients.

BARHEMSYS® is manufactured in Italy pursuant to an agreement between the Operating Company and Patheon UK Limited ("**Patheon**"). The Group currently relies on Patheon's ability to effectively scale production, with annual volume expected to increase from 1,875,000 vials in 2019 to 3,200,000 vials in 2020. Any inability by Patheon to successfully scale production to higher volume or to do so safely and in compliance with applicable regulations, or any delay or disruption in the supply of the API or other components for its products, could cause delays to the Group's commercialisation efforts and the Group may not be able to sufficiently replace or supplement manufacturing capacity. Any impact on commercialisation of BARHEMSYS® could reduce potential revenues from sales thereof and could adversely affect the Group's business.

BYFAVO™ is also manufactured in Italy by Patheon pursuant to an agreement between Patheon and Cosmo. The Group is currently negotiating for such agreement to be novated to its benefit. The terms of such novation are under discussion, which may include certain amendments to the terms of the existing BYFAVO™ manufacturing arrangements between Patheon and Cosmo. Such an agreement may not be reached on advantageous terms, or at all, and any dispute relating thereto could interrupt or delay manufacturing of BYFAVO™ or increase the costs of producing BYFAVO™ moving forward, affecting the Group's ability to raise revenues from its commercialisation and adversely affecting its business. There is no agreement in place between the Company and Cosmo with respect to an obligation to procure the manufacture of BYFAVO™ and, until the novation agreement (referred to above) comes into effect, the Company has no rights to pursue Patheon if there is a breach or other supply disruption under the current contractual arrangements between Patheon and Cosmo. The Company currently has no ability to procure the supply of BYFAVO™ nor can it assure the compliance by Cosmo of its contractual obligations to Patheon.

Furthermore, reliance on third party manufacturers, such as Patheon and Icrom, entails risks, including risks related to such parties' regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreements by the third parties because of factors beyond the Group's control and the possibility of termination or non-renewal of the relevant agreements by the third party manufacturers at a time that is costly or damaging to the Group. In addition, the FDA and other regulatory authorities require that product candidates and any products that the Group commercialise be manufactured according to current Good Manufacturing Practices ("**cGMPs**") and similar international standards. For example, the approval by the FDA of BARHEMSYS® was delayed due to pre-approval inspection issues identified at a third party manufacturer of API. Whilst those issues were resolved prior to approval of BARHEMSYS® and a second API supplier has been approved, any subsequent failure by appointed third party manufacturers to comply with cGMP could lead to a delay in, or failure to obtain, regulatory approval of any of the Group's other product candidates. In addition, such failure could be the basis for the FDA or other regulatory authorities to issue a warning or untitled letter, withdraw previously granted approvals for products or take other regulatory or legal action, including recall or seizure, total or partial suspension of production, suspension of ongoing clinical trials, refusal to approve pending supplemental applications, detention of a product, refusal to permit the import or export of products, injunction, or the imposition of civil and criminal penalties.

Any significant disruption in supplier relationships could materially adversely affect the Group's business.

The Group sources key materials necessary for the manufacture and formulation of the Group's products, including amisulpride (which is the active ingredient for both BARHEMSYS® and APD403) and remimazolam (which is the active ingredient for BYFAVO™) from third party suppliers, either directly or indirectly through its manufacturers. There are a limited number of suppliers for certain processes and for key materials. For example, the API for BARHEMSYS® is currently supplied to the Operating Company by Icrom and the API for BYFAVO™ is currently supplied by a single source supplier, Cambrex Corporation. Currently the Group does not have a direct supply arrangement in place for remimazolam (which is the active ingredient for BYFAVO™). However, under the BYFAVO™ Head-Licence Agreement between Cosmo and Paion to develop and commercialise BYFAVO™ (which was assigned to the Operating Company with effect from 7 August 2020), Paion has agreed that, until a commercial product supply agreement is concluded for the supply of remimazolam by a third party contract manufacturing organisation,

Paion will deliver the API to the Operating Company at cost, which may be via Paion's remimazolam contract manufacturing organisation.

Such suppliers may not sell services or key materials to the Group or its manufacturers at the times they are needed or on commercially reasonable terms. The Company would be unable to obtain certain raw materials, other products, or services for an indeterminate period of time if any of these third parties were to cease or interrupt production or otherwise fail to supply these materials, products, or services to if for any reason, including due to regulatory requirements or actions (including recalls), adverse financial developments at or affecting the supplier, failure by the supplier to comply with cGMPs, contamination, business interruptions, or labour shortages or disputes. While the Company is always looking to diversify its supply chain, including for alternative sources of API, it may be unsuccessful in engaging backup or alternative suppliers or service providers in a timely manner or at all.

Any significant delay in the supply of key materials needed to produce a product candidate for any ongoing clinical study could considerably delay completion of the study, product testing and potential regulatory approval of the relevant product candidate.

If the Group is unable to purchase relevant key materials for BARHEMSYS® and BYFAVO™ or other commercialisation-stage products, the commercial launch of such products could be delayed or there could be a shortage in supply, which could impair the Group's ability to generate revenues from the sale of the product. For instance, the Group relies on the supply of specialised single-use glass vials for BARHEMSYS® and BYFAVO™. A shortage in the availability of glass, and in turn the supply of such vials, including as the result of any global immunisation efforts in connection with the response to COVID-19, could lead to such delays and delay commercialisation.

The Group is dependent on licensed intellectual property, and if it were to fail to comply with its obligations under its existing and any future intellectual property licences with third parties, it could lose license rights that are important to its business and it may not be able to continue developing or commercialising its products.

The Group is dependent on licensed intellectual property, and if it were to fail to comply with its obligations under its existing and any future intellectual property licences with third parties, it could lose licence rights that are important to its business and it may not be able to continue developing or commercializing its products.

The Group is party to an in-licensing agreement with Paion, pursuant to which it has in-licenced exclusive rights to BYFAVO™, which is important to the Group's business strategy. The Group may enter into additional licence agreements in the future. The license agreement with Paion imposes, and the Directors expect that future licence agreements may impose: (i) obligations to diligently develop and/or commercialise the in-licensed technology; (ii) obligations to pay milestone payments; (iii) obligations to pay royalty payments; (iv) requirements as to insurance; and (v) other Group obligations. Any uncured, material breach under the BYFAVO™ Assignment Agreement could result in the Group's loss of rights to BYFAVO™ and other intellectual property licensed to it, and could compromise its development and commercialisation efforts for its current or any future products.

RISKS RELATING TO THE GROUP'S BUSINESS ACTIVITY AND INDUSTRY

The Group's business has been adversely affected by the recent COVID-19 outbreak and may experience further adverse effects. The COVID-19 pandemic will likely continue to materially affect the Group's operations as well as the business or operations of our manufacturers, contract research organisations (CROs) or other third parties such as healthcare settings with whom it conducts business.

On 11 March 2020, the World Health Organisation announced that the outbreak of COVID-19 (commonly referred to as Coronavirus) had been declared a global pandemic. The long-term impacts of the outbreak are unknown and rapidly evolving. The widespread health crisis has adversely affected the global economy, resulting in a substantial decline in financial markets. The future development of the outbreak is highly uncertain and there is no assurance that the outbreak will not have a material adverse impact on the future results of the Company. The extent of the impact will depend on the geographical range of the virus, infection rates, the severity and mortality rates of the virus, the timing and efficacy of a vaccine, the effectiveness of virtual means of marketing and communicating in commercialising the Group's products, access to hospital premises and personnel responsible for overseeing hospital formularies, the steps taken nationally and globally to prevent the spread of the virus as well as fiscal and monetary stimuli offered by governments globally.

If the negative impact from the COVID-19 pandemic continues, the Group's results may be worse than expected. The full extent of the impact will depend on future developments, such as the ultimate duration and the severity of the spread of COVID-19 in the US and globally, the effectiveness of federal, state, local and foreign governments' mitigation actions, together with the pandemic's impact on the US and global economies. Even if government measures intended to control spread of the virus are reduced, hospital settings may continue to restrict access to their premises or have reduced resources and availability as a result of the virus.

Whilst the FDA approved BARHEMSYS® for marketing in the US on 26 February 2020, the Group had to adjust its commercialisation strategy for BARHEMSYS® and delay some of the previously planned launch activities as a direct result of COVID-19 owing to restricted access to healthcare settings and the postponement of medical conferences. The commercialisation strategy for BYFAVO™ has also been adjusted to accommodate the current environment. Continued restricted access to healthcare settings may have a material adverse effect on the Company's ability to commercialise its approved products which will negatively affect its business and results of operations. Further, during the crisis in the US, the majority of hospitals have postponed or cancelled all unnecessary and elective surgeries. There is a risk that the continued impact of COVID-19 in the US may result in further surgical postponements and cancellations, thereby limiting uptake and market acceptance. This would further delay the Group's ability to successfully commercialise its products. It is possible that the negative effect on hospital profitability due to cancelled and delayed procedures could have a negative effect on hospital pharmacy budgets at some institutions which could affect product demand.

The Group has temporarily suspended in-person interactions by its customer-facing (field) personnel in healthcare settings and moved to a remote engagement model in the US. A number of hospitals have restricted access to essential personnel. It is possible that these actions could have a greater negative impact on its business than currently expected. It is also possible that there could be a longer-lasting shift in interactions between field personnel and health care professionals that the Directors have not anticipated, which could have a negative impact on the Group's business and results of operations.

Although the Directors currently do not anticipate any disruption to the supply of the Group's medicines to patients, it is possible that the Group could experience manufacturing or supply issues due to COVID-19 in the future, which would increase the negative impact on the Group's business and results of operations. In addition, if a natural disaster or other potentially disruptive event occurs on top of the current pandemic, it could deplete the Group's reserve stock levels and the Group could experience a manufacturing or supply issue.

The commercial success of BARHEMSYS® and BYFAVO™ and any of the Group's other future products will depend on the rate and degree of market acceptance of these products among physicians, patients, healthcare payors, group purchasing organisations and the medical community.

The commercial success of BARHEMSYS® and BYFAVO™ and any of the Group's future products will depend upon the acceptance of such products as safe and effective by the medical community and patients and the products' pharmoeconomic benefits. In particular, BARHEMSYS® and BYFAVO™ will not generally be available for use by surgical teams until accepted by their hospital's pharmacy and therapeutics (P&T) committee and included on the formulary of approved products within that hospital. The rate and speed of acceptance will directly impact on the commercial success of each product. The market acceptance of the Group's products could be affected by a number of other factors, including:

- the safety and efficacy of the products, as well as the acceptance by physicians and patients of the products as safe and effective;
- the cost-effectiveness and availability of coverage on formularies for the products;
- the availability and terms of contracts with group purchasing organisations;
- the success of existing products addressing the Group's target markets or the emergence of equivalent or superior products;
- changes in the standard of care for the targeted indications for any product candidate;
- sales, marketing and distribution support;
- potential product liability claims;
- relative convenience, ease of administration and other perceived advantages over alternative products and therapies;

- the resources and the effectiveness of potential partners;
- prevalence and severity of adverse events or publicity;
- limitations, precautions, warnings and other wording in the summary of product characteristics, patient information leaflet, package labelling or instructions for use;
- the Group's ability to enter into any licensing and/or distribution agreements for BARHEMSYS® and APD403 outside the United States or receive payments thereunder (e.g., royalty payments for licenced products) and receive any necessary consents under its debt covenants, regulatory approvals and product agreements, relating thereto;
- any disputes with prospective partners or future partners with whom the Group enters into a licensing and/or distribution agreement, including disagreements over proprietary rights or contract interpretation that might disrupt the Group's commercialisation outside the United States or lead prospective partners to develop a competing product; and
- in the case of APD403 and any of the Group's future products, the timing of receipt of marketing approvals.

In addition, market acceptance depends on the effectiveness of the Group's marketing strategy, and, to date, the Group has not engaged in sales or marketing. Efforts to educate the medical community and healthcare payors on the benefits of the Group's products may require significant resources and may never be successful. For example, management has concluded based on their assessment of the market that there have not been any new treatments for PONV since the launch of Emend® in 2009. As a result, the unmet medical need for new treatments for PONV may be less understood among physicians and others in the medical community and may therefore result in a relatively slow sales ramp-up and require significant resources (including investments in the marketing and sales force). If the medical community and patients do not ultimately accept the benefits of the Group's products, the Group's business, prospects, financial condition and results of operations could be materially and adversely affected.

It is difficult for a prospective investor to evaluate the Group's ability to commercialise products successfully and to assess the Group's future prospects. The Group's ability to generate future revenues and become profitable will depend upon its ability to successfully commercialise BARHEMSYS®, BYFAVO™ or APD403.

The Group's activities to date have been limited to staffing, business planning, raising capital, developing its technology, identifying potential product candidates, securing intellectual property, undertaking or managing pre-clinical studies, clinical studies, seeking regulatory approval and preparatory work for the US launch of BARHEMSYS® and BYFAVO™. The Group has not yet demonstrated its ability to conduct sales and marketing activities necessary for successful product commercialisation. There can be no assurance that the Group will be successful in transitioning to commercialisation. The lack of any history of successful product commercialisation makes it difficult for a prospective investor to evaluate the Group's ability to achieve its business plans. Additionally, given the anticipated transition to commercialisation, the Group's past results of operations are in many respects not indicative of the Group's results going forward, which makes it difficult for a prospective investor to assess the Group's future prospects. Any predictions about the Group's future success, performance or viability may not be as accurate as they might be if the Group had an established sales channel or established products on the market.

The success of the Group's business is dependent upon its ability to commercialise its products. The Group's ability to generate revenue from BARHEMSYS®, BYFAVO™ and any other approved products will also depend on a number of additional factors, including its ability to:

- achieve a commercially viable price for its approved products;
- obtain commercial quantities of its approved products at acceptable cost levels;
- achieve inclusion of its products on hospital formularies;
- develop a commercial organisation capable of (and if successful in doing so, then achieving) sales, marketing and distribution in the US; and
- find suitable distribution partners to market, sell and distribute the Group's approved products in markets outside the US (and receipt of any necessary consents under its debt covenants, regulatory approvals and product agreements relating thereto).

The Group does not have a fully established sales or marketing infrastructure and has not been engaged in the sale or marketing of pharmaceutical products.

To achieve commercial success for any approved product, the Group must complete the development of its sales and marketing organisation. The Group is currently establishing its own sales and marketing capabilities to promote both BARHEMSYS® and BYFAVO™ in the US with a targeted sales force. There are risks and expenses involved with establishing the Group's own sales and marketing capabilities and entering into arrangements with third parties to perform these services.

Factors that may inhibit the Group's efforts to commercialise its products on its own include:

- the Group's inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of anaesthetists and/or other physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put the Group at a competitive disadvantage relative to companies with more extensive product portfolios;
- unforeseen costs and expenses associated with creating an independent sales and marketing organisation; and
- costs of marketing and promotion above those anticipated by the Group.

The Group may fail to launch its products effectively or to market its products effectively given its limited experience in the sales and marketing of pharmaceutical products. In addition, recruiting and training a sales force is expensive and time consuming and delays in building the sales force could adversely impact any product launch. In the event that any such launch is delayed or does not occur for any reason, the Group would have prematurely or unnecessarily incurred these commercialisation expenses, and the Group's investment would be lost if it cannot retain or reposition its sales and marketing personnel.

While the Group does not intend to outsource these functions at this time, if in the future the Group enters into arrangements with third parties to perform sales and marketing services, the Group's product revenues or the profitability of these product revenues to the Group could be lower than if the Group were to market and sell any products that it develops itself. In addition, the Group may not be successful in entering into arrangements with third parties to sell and market its products or may be unable to do so on terms that are favourable to the Group. Acceptable third parties may fail to devote the necessary resources and attention to sell and market the Group's products effectively. If the Group does not establish sales and marketing capabilities successfully, either on its own or in collaboration with third parties, it will not be successful in commercialising its products, which in turn would have a material adverse effect on its business, prospects, financial condition and results of operations.

Further, even if the Group generates revenues from the sale of approved products, it may not become profitable. If the Group fails to become profitable or is unable to sustain profitability on a continuing basis, then it may need to obtain additional funding to continue operations or be forced to reduce operations or discontinue operations altogether.

The Company may be unsuccessful in evaluating material risks involved in completed and future acquisitions and in-licensing arrangements and may be unable to realise anticipated benefits or synergies.

Earlier this year, the Company completed the BYFAVO™ Acquisition and regularly reviews acquisition and in-licensing opportunities. As part of such review, the Company conducts business, legal and financial due diligence with the goal of identifying and evaluating material risks involved in any acquisition or in-licensing arrangement. Despite the Company's efforts, it may be unsuccessful in identifying and/or evaluating all such risks.

There can be no assurance that the Company will be able to realise synergies from the BYFAVO™ Acquisition in the anticipated amounts or within anticipated time frames, or at all. The Company anticipates that the commercialisation of BYFAVO™ in the United States will coincide with the commercialisation of BARHEMSYS® and may implement cost saving initiatives including leveraging the commercialisation infrastructure the Company intends to build such that it can be utilised for both BARHEMSYS® and BYFAVO™. In addition, the Company anticipates that successful establishment of BYFAVO™ and BARHEMSYS® in the United States may create a US hospital sales and marketing infrastructure for future complementary products or product candidates. The Company will incur costs to establish such infrastructure and, if the products have different target users and customers than the Company anticipates, if its sales

representatives' training and relationships favour one product or the other, or if other factors develop, the Company may not ultimately successfully leverage such infrastructure across products or achieve the synergies anticipated. In addition, these or any other costs or synergies that the Company may realise from completed and future acquisitions and in-licensing arrangements may differ materially from the Company's estimates and expectations. In addition, any synergies that the Company may realise could be offset, in whole or in part, by reductions in revenues or through increases in other expenses. Neither the Company's independent auditors nor any other independent auditors, are likely to examine, compile or perform any procedures with respect to possible synergies, nor are they likely to express any opinion, or any other form of assurance on such information or their achievability. Assumptions relating to cost or other synergies involve subjective decisions and judgments.

The Group faces potential competition, which may result in others discovering, developing or commercialising substantially equivalent or competing products before, or more successfully than, the Group.

The development and commercialisation of new drugs is highly competitive and the Group faces competition with respect to its current product candidates. There may be pharmaceutical and biotechnology companies that could be pursuing the development of competitive products of which the Group is presently unaware. Potential competitors also include academic institutions, government agencies and other public and private research organisations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialisation of competing products.

More established competitors may have a competitive advantage over the Group due to their greater size, cash flows and institutional experience. Compared to the Group, many of its potential competitors may have significantly greater financial, technical and human resources and may be more successful in developing and/or in manufacturing and marketing their products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of the Group's existing or potential competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. The Group's competitors may compete with it in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject enrolment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the Group's product development programmes.

As a result of these factors, the Group's existing or potential competitors may obtain regulatory approval of their products more rapidly than the Group or may obtain patent protection or other intellectual property rights that limit the Group's ability to develop or commercialise its product candidates.

At the product level, the Group faces competition from both existing products and newly developed products. The Group's product candidates have been and continue to be developed for surgical and cancer patient care as well as other invasive medical procedures. There are existing therapies and supportive care products marketed for such patients and many of the products are genericised. In many cases, these drugs are administered in combination to enhance efficacy or to reduce side effects. Many of these approved drugs are well-established therapies or products and are widely accepted by physicians. The Group expects its currently approved products, BARHEMSYS® and BYFAVO™, to be priced at a premium to the price of existing generic products. This may make it difficult for the Group to gain market share either alongside or in substitution for existing therapies and supportive care products and, consequently, to achieve expected revenue levels from its approved products. The Group's competitors may also develop new drugs that are more effective and/or less costly than the Group's products, which could result in such competing products being more widely adopted and used than the Group's products.

Should the Group be unsuccessful in responding to competition in the development, manufacturing and marketing of its products, or in having its products gain market share alongside or in substitution for existing therapies and products for surgical and cancer supportive care, as well as other invasive medical procedures, this could have a material adverse effect on the Group's business, financial condition, results of operations and prospects.

As the Group's products or product candidates are commercialised, they may become subject to unfavourable pricing regulations or healthcare reform initiatives, which could be detrimental to the Group's business.

The regulations that govern drug approvals and marketing authorisations as well as pricing and reimbursement for new drugs vary widely from country to country. In the US, changes in legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining regulatory approvals. If, in the future, the Company determines to seek marketing authorisation and commercialise its products in other jurisdictions, some countries (such as the UK, France and Italy) may

require approval of the sales price before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In certain markets outside the US, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, the Group expects that, in certain countries, even if it obtains marketing approval for a product it will be subject to further price regulations that may delay the commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues that can be generated from the sale of the product in that particular country. Adverse pricing limitations may hinder the Group's ability to recoup its investment in one or more product candidates even if the product candidates obtain marketing approval.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices. The Group's inability to promptly obtain profitable pricing levels for any of its approved products could have a material adverse effect on its ability to raise capital needed to commercialise products and the overall business, financial condition, results of operations and prospects of the Group.

The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs.

The Group's future performance depends on, among other things, the accuracy of its estimates of the Group's market position, the size of its addressable market and estimated revenues from sales of its products and profit margin related thereto. The Group and the Directors rely on market, industry and scientific data for the research and development of its products and to develop plans for commercialisation of its products and, in addition, the Group conducts its own internal analyses based on qualitative and quantitative data, the experience of management in the commercialisation of other products, managements' knowledge of the market and market participants and certain assumptions related to expenses, pricing, competition and other factors to develop its commercialisation plan and related budget. For example, the Group has made, and expects to make, strategic commercialisation decisions based upon, among other data, internal Company estimates of the Group's market position and the size of its addressable market. To estimate its market position and the size of its addressable market, the Group relies on certain assumptions and estimates of the number of patients requiring treatment based on data on the number of surgeries or other procedures that are conducted. Some of this information is obtained from third party publications and surveys, some of which are not updated regularly, resulting in the Company relying on information released over five years, and in some cases ten years, prior to the date of this Prospectus. As such there is a possibility that the data produced by third parties, while accurately reproduced by the Company, may not be entirely accurate or reliable. As a result, estimates of the total addressable market or the anticipated volume of sales of the Group's products may vary materially due to unreliability of the underlying data or the inaccuracy of certain assumption described above. The Group's anticipated sales, and therefore revenues, could be lower than expected if the addressable market is smaller than expected, or costs could be greater to market the Group's products due to inaccurate estimates of market size. Any inaccuracy in the Group's estimates related to its addressable market or market size or in the Company's commercialisation plan and related budget, could adversely affect the Company's business, financial condition and prospects.

LEGAL AND REGULATORY RISKS

The Group will be subject to ongoing regulatory obligations and review by the FDA in particular and may still face future development and regulatory difficulties, which may result in additional expenses or the Group being subjected to sanctions or penalties for failure to comply with its regulatory obligations.

Even following regulatory approval for a product, the Group will be subject to ongoing regulatory requirements governing the manufacture, quality control, further development, labelling, packaging, storage, distribution, safety surveillance, import, export, advertising and promotion of the product, recordkeeping and reporting of safety and other post-market information. The safety profile of any product will continue to be monitored closely by regulatory authorities after approval and the Group is itself required to monitor the safety profile of its products and to report issues to the regulatory authorities. Drug safety risks which could lead to product withdrawal from the market can occur several years after FDA approval. There is no guarantee that BARHEMSYS®, BYFAVO™ or APD403 are going to be as effective and safe as assessed to be by the FDA on the basis of premarket clinical evidence. Published academic clinical research results upon which the efficacy, quality and safety properties of BARHEMSYS® for example are based may at a later date be proven to be technically incorrect. The occurrence of such an event would lead to significant doubt on the scientific validity of any FDA approval. If the regulatory authorities become aware of new

safety information after approval of any of the Group's product candidates, they may require labelling changes or impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. In addition, manufacturers of products and their facilities are subject to continual review and periodic inspections by the regulatory authorities for compliance with cGMP requirements. If the Group or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or the Group, including recall or withdrawal of the product from the market or suspension of manufacturing. If the products or the manufacturing facilities for the products fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- issue untitled letters, which cite violations not meeting the threshold of a warning letter;
- mandate modifications to promotional materials or require the Group to provide corrective information to healthcare practitioners;
- require the Group to enter into a consent decree, which can include imposition of various fines, reimbursement for inspection costs, required remedial actions by specific dates and penalties for non-compliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical studies;
- refuse to approve pending applications or supplements to applications filed;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require the Group to initiate a product recall.

The occurrence of any of the regulatory actions or incurrence of any of the penalties set out above may inhibit the Group's ability to commercialise its products and, consequently, could materially adversely affect the Group's business, financial condition, results of operations and prospects.

The Group will be subject to ongoing obligations and continued regulatory review in respect of its approved products, which may result in significant additional expense. Additionally, the Group's approved products could be subject to labelling and other restrictions and withdrawal from the market and the Group may be subject to penalties if it fails to comply with regulatory requirements or if it experiences unanticipated problems with its approved products.

The Group's approved products will be subject to ongoing regulatory requirements governing their manufacture, labelling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and the reporting of adverse events and other post-market information. In addition, the third party manufacturers of the Group's approved products will be subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. In addition, the Group's product labelling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review.

If the Group or a regulatory agency discovers previously unknown problems with an approved product, such as adverse events of unanticipated severity or frequency, problems with the facility where the product is manufactured, or the Group's third party manufacturers fail to comply with applicable regulatory requirements, the Group may be subject to the following administrative or judicial sanctions:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- issuance of warning letters or untitled letters;
- injunctions or the imposition of civil or criminal penalties or monetary fines;
- suspension or withdrawal of regulatory approval;
- suspension of any ongoing clinical trials;

- refusal to approve pending applications or supplements to approved applications filed by the Group, or suspension or revocation of product licence approvals;
- suspension or imposition of restrictions on operations, including costly new manufacturing requirements; or
- product seizure or detention or refusal to permit the import or export of product.

The occurrence of any event or penalty described above may inhibit the Group's ability to commercialise its products and generate revenue. Adverse regulatory action may also potentially lead to product liability claims and increase the Group's product liability exposure.

Moreover, the FDA approval of BYFAVO™ is subject to completion of scheduling under the Controlled Substances Act by the Drug Enforcement Administration. Any failure to achieve scheduling may inhibit the Group's ability to commercialise BYFAVO™ and, consequently, could materially adversely affect the Group's business, financial condition, results of operations and prospects.

The ability of the Group to commercialise APD403 or any future products or product candidates is dependent on gaining regulatory approval. The Group is subject to the risk that it will be unable to obtain such regulatory approvals, that the scope of any approvals it does receive is limited or that further clinical or preclinical studies may be required.

The ability of the Group to commercialise APD403 or any future products or product candidates is dependent on gaining regulatory approval. It is possible that APD403 or any future products or product candidates (including any product candidates that it may in-license or acquire and seek to develop in the future), may not obtain regulatory approval in any or all jurisdictions where the Group seeks it.

Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary across jurisdictions. The FDA or other regulatory authorities may require further information, including additional pre-clinical or clinical data to support approval, which may delay or prevent altogether such approval and, consequently, the Group's commercialisation plans.

Any approval from the FDA or other relevant regulatory authorities might be for fewer or more limited indications than requested, be for a label that does not include the labelling claims necessary or desirable for the successful commercialisation of that product candidate, contain significant limitations related to use for certain age groups, warnings, precautions or contraindications, or be contingent upon onerous or costly post-marketing clinical trials, approval studies or risk management requirements, any of which could require further work for the Group with additional expenditure and associated delays to secure the desired label.

Any drug could fail to receive regulatory approval from regulatory authorities for many reasons, including:

- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement by regulatory authorities with the Group's interpretation of data from pre-clinical studies or clinical trials;
- insufficiency of data collected from clinical trials of the Group's product candidates to support the submission and filing of an NDA or other submission;
- lack of approvals of the manufacturing processes or facilities of third party manufacturers or active ingredient suppliers with whom the Group contracts for clinical and commercial supplies;
- changes in the approval policies or regulations that render the Group's pre-clinical and clinical data insufficient for approval;
- failure to reach agreement on the design or scope of the clinical trials;
- failure of clinical trials to meet the level of statistical significance required for approval; or
- failure to demonstrate that a product candidate is safe and effective for its proposed indication.

If the Group is unable to obtain regulatory approval in any territory, but in particular the United States, for any product candidate or any approval contains significant limitations or is materially delayed, it may not be able to continue its operations, or it may not be able to obtain sufficient funding or generate sufficient revenue to become profitable, or to continue the development of APD403 or any other product candidate that the Group may discover, in-license or acquire in the future.

Success in pre-clinical testing and early clinical studies does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of an investigational drug. A number of companies in the pharmaceutical industry, including those with greater resources and experience than the Group, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier clinical trials. Despite the results reported in earlier clinical trials for APD403, it is uncertain whether future clinical trials will demonstrate adequate efficacy and safety to support regulatory approval to market any of the product candidates in any particular jurisdiction or jurisdictions.

Successful completion of appropriately designed clinical trials is an essential element of obtaining regulatory approval for product candidates. Subject enrolment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the subject population, the proximity of subjects to trial sites, the eligibility criteria for the clinical trial, the design of the clinical trial, inability to obtain and maintain subject consents, the risk that enrolled subjects will drop out before completion of the clinical trial, competing clinical trials and clinicians' and subjects' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications being investigated. Patients recruited for clinical trials must give their informed consent and the trial must be conducted in accordance with Good Clinical Practice (GCP) standards. Furthermore, the Group relies on CROs and clinical trial sites to ensure the proper and timely conduct of its clinical trials and, while it has agreements governing the CROs' committed activities, the Group has limited influence over their actual performance.

If material delays are experienced in the completion of any clinical trial, or clinical trials are terminated prematurely or fail to demonstrate the required benefits of one or more product candidates, the commercial prospects of those product candidates will be adversely affected, and the ability to obtain regulatory approval and, ultimately, to commercialise and generate product revenues from those product candidates will be delayed or may never be realised. In addition, any delays in completing clinical trials may increase the Group's operating costs, slow product candidate development and the regulatory approval process and jeopardise the ability to commence product sales and generate revenues. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of the product candidates. Any of these occurrences may adversely affect the Group's business, financial condition, results of operations and prospects.

Potential product liability lawsuits against the Group could cause the Group to incur substantial liabilities and limit commercialisation of any products that the Group may develop and there can be no certainty that the Group can obtain adequate product liability insurance in order to protect it from potential claims.

The sale of any products for which the Group obtains marketing approval, including BARHEMSYS® and BYFAVO™, and the use of product candidates in clinical trials expose the Group to the risk of product liability claims. Future product liability claims might be brought against the Group by consumers, healthcare providers, pharmaceutical or biotechnology companies or others selling or otherwise coming into contact with the Group's products. On occasion, large judgments have been awarded in class action lawsuits based on therapeutics that had unanticipated adverse effects. If the Group cannot successfully defend against product liability claims, the Group could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of the Group's business reputation and significant negative media attention;
- withdrawal of participants from the Group's clinical trials;
- significant costs to defend the related litigation;
- diversion of management's attention from the Group's primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialise the Group's products or any product candidate;
- product recalls, withdrawals or labelling, marketing or promotional restrictions;
- decreased demand for the Group's products or any product candidate, if approved; and
- loss of revenue.

The Group intends to acquire insurance coverage to include the sale of commercial products if it is economical to do so (given the level of premiums and the risk and magnitude of potential liability). However, insurance coverage may be expensive and the Group may be unable to obtain product liability

insurance on commercially reasonable terms or in amounts sufficient to reimburse the Group for any expenses or losses the Group may suffer. A successful product liability claim or series of claims brought against the Group, if judgments exceed the Group's insurance coverage, could materially and adversely affect the Group's business, prospects, financial condition and results of operations, including preventing or limiting the commercialisation of any product candidates the Group develops.

The Group has incurred increased costs as a result of operating as a public company and management is required to devote substantial time to compliance initiatives and regulations.

As a public company, the Company incurs significant legal, accounting and other expenses to comply with securities rules and regulations that it did not incur as a private company. However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. Management and other personnel also devote time to compliance initiatives, diverting their attention from other activities. Moreover, compliance requirements and regulations have increased legal and financial costs substantially and make some activities more time-consuming and costly. The increased costs have and will continue to increase the Group's consolidated net loss or reduce its net profit. Management cannot predict or estimate the amount or timing of additional costs that may be incurred to respond to these requirements.

Recent developments relating to the United Kingdom's withdrawal from the European Union could adversely affect the Group.

The United Kingdom held a referendum on 23 June 2016 in which a majority voted for the United Kingdom's withdrawal from the European Union, or Brexit. As a result of this vote, on 29 March 2017 the United Kingdom officially started the separation process. Following negotiations on the terms of the United Kingdom's exit from the European Union, a withdrawal agreement ("**Withdrawal Agreement**") setting out the terms of the exit was entered into on 24 January 2020. The Withdrawal Agreement became effective, and the United Kingdom formally left the European Union, on 31 January 2020. Although the United Kingdom has officially exited the European Union, the pre-31 January 2020 legal status quo is continuing during a so-called "transition period" during which the United Kingdom and the European Union are continuing to negotiate the terms of their future relationship including any future trade agreement.

The effects of Brexit have been and are expected to continue to be far-reaching. Brexit and the perceptions as to its impact may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial and foreign exchange markets. Brexit could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and the European Union; however, the full effects of Brexit are uncertain and will depend on any agreements the United Kingdom may make to retain access to European Union markets.

In addition, the Group expects that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European Union laws to replicate or replace. If the United Kingdom were to significantly alter its regulations affecting the pharmaceutical industry, the Group could face significant new costs. It may also be time-consuming and expensive for the Group to alter its internal operations in order to comply with new regulations. It is unclear at this time what Brexit's impact will have on the Group's intellectual property rights and the process for obtaining, maintaining and defending such rights. It is possible that certain intellectual property rights, such as trademarks, granted by the European Union will cease being enforceable in the United Kingdom absent special arrangements to the contrary, and the Group may be required to refile its trademarks and other intellectual property applications domestically in the United Kingdom. As a result of Brexit, other European countries may seek to conduct referenda with respect to their continuing membership in the European Union. Given these possibilities and others the Directors may not anticipate, as well as the lack of comparable precedent, the Directors cannot be certain of the full extent to which Brexit could adversely affect the Group's business, results of operations and financial condition.

Changes in tax laws or in the policy of tax administrations, including changes in the interpretation or application of existing tax laws, may adversely affect the Group's profitability.

Changes in tax laws or in the policy of tax administrations, including changes in the interpretation or application of existing tax laws, may adversely affect the Group's profitability. The Group operates in both the United Kingdom and the United States and is therefore subject to differing tax regimes. Tax laws, and the interpretation of tax laws by tax authorities, frequently change, sometimes with retrospective effect. It is

possible that tax laws and the interpretation and/or application of such laws may change in such a way that the Group's effective corporate tax rates are increased, that the Group's recoverability of value added tax (or tax of a similar nature) is decreased or that social security costs and other taxes directly borne by the Group are increased. For the foregoing reasons, changes in tax law policy or administration, could have a material adverse effect on business, results of operations, financial condition and/or prospects of the Group.

RISKS RELATED TO THE GROUP'S INTELLECTUAL PROPERTY

An inability to protect its intellectual property rights could harm the Group's competitive position.

The Group's commercial potential depends on its ability to protect its intellectual property relating to its product candidates and products. It relies and will in the future rely on trade secret, patent (and, if available, supplementary protection certificates), copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection.

In particular, the Group's longer-term commercial success depends largely on its ability to obtain and maintain patent protection with respect to its product candidates and products in the US and in other jurisdictions. The patent (and where available the supplementary protection certificate) positions of pharmaceutical companies generally are uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of the Group's patents, including those patent rights licensed to the Group by third parties, and the protection that might become available as a result of the grant of supplementary protection certificates, are uncertain.

The Group has various patents granted and pending in a number of jurisdictions in respect of BARHEMSYS® and APD403. The Group has also acquired rights to patents granted and pending in the US in respect of BYFAVO™. However, the rights already granted under any of the Group's currently issued patents and those that may be granted under future issued patents may not provide it with the proprietary protection or competitive advantages it is seeking. If the Group is unable to obtain and maintain patent protection for its product candidates and products, or if the scope of the patent protection obtained is not sufficient, competitors could develop and commercialise products similar or superior to those of the Group, and its ability to successfully commercialise its products may be materially adversely affected. In addition, if patent term extensions and/or supplementary protection certificates are not available upon expiry of any of the Group's patents, competitors may be able to commercialise the products themselves earlier than they would have otherwise been able to do and the Group's ability to successfully commercialise its products may be materially adversely affected.

With respect to patent rights, the Group's management does not know whether any pending patent applications for product candidates will result in the issuance of patents, or whether such patents when issued will effectively prevent others from commercialising competitive technologies and products. Because the issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability, issued patents that are owned or have been licensed from third parties may be challenged in the courts or international patent offices. Although the Group has not faced such challenges on its existing granted patents to date, there can be no assurance that such challenges will not arise in the future. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents, or the invalidity or unenforceability of such patents, which could limit the Group's ability to prevent others from using or commercialising similar or identical technology and products, or limit the duration of the patent protection for its technology and products.

The patent prosecution process is expensive and time-consuming and the timing unpredictable, and the Group, or a licensor, may not be able to file and execute all necessary or desirable patent applications at a commercially reasonable cost or in a timely manner which may adversely affect the commercial value of the Group's product candidates. It is also possible that the Group or its licensors will fail to identify patentable aspects of inventions made in the course of development and commercialisation activities before it is too late to obtain patent protection for them. Further, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialised and supplementary protection certificates may not be granted to the Group for such products.

Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications are typically not published until 18 months after filing, or in some cases not at all. Therefore, the Group cannot be certain that it is the first to make the inventions claimed in owned or licensed patents or pending patent applications, or that the Group or its licensors were the first to file for patent protection

of such inventions. The Group is therefore subject to the risk that other parties will have superior claims for patent protection unknown to the Group at the time it files for patent protection that result in the Group's application being unsuccessful.

Protecting against the unauthorised use of patented technology and other intellectual property rights is expensive, difficult and may, in some cases, not be possible. In some cases, it may be difficult or impossible to detect third party infringement or misappropriation of intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

The Group may become involved in litigation to protect or enforce its intellectual property, which could be expensive, time-consuming and ultimately, unsuccessful.

Competitors may infringe the Group's patents or misappropriate or otherwise violate the Group's intellectual property rights. To counter infringement or unauthorised use, litigation may be necessary in the future to enforce or defend intellectual property rights, to protect trade secrets or to determine the validity and scope of intellectual property rights or the proprietary rights of others. Although the Group has not been involved in any such litigation to date, to the extent such litigation arises it can be expensive and time-consuming. Many of the Group's current and potential competitors have the ability to dedicate substantially greater resources to defend their intellectual property rights than the Group does. Accordingly, despite reasonable efforts, the Group may not be able to prevent third parties from infringing upon or misappropriating its intellectual property. Litigation could result in substantial costs and diversion of management resources, which could materially adversely affect the Group's business and results of operations. In addition, in an infringement proceeding, a court may decide that patents owned by or licensed to the Group are invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that the Group's patents do not cover the technology in question or that the patents should not have been issued. An adverse result in any litigation proceeding could put one or more Group patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some Group confidential information could be compromised by disclosure during this type of litigation. Due to all of the above, litigation in connection with protecting the Group's intellectual property rights, whether or not ultimately decided in the Group's favour, could have a material adverse effect on the Group's business, financial condition, results of operations and prospects.

Third parties may initiate legal proceedings alleging that the Group is infringing their intellectual property rights, the outcome of which may be uncertain and could have a material adverse effect on the Group's business and prospects.

The Group's commercial success will depend upon the Group's ability and the ability of its collaborators to develop, manufacture, market and sell its product candidates and to use proprietary technologies without infringing the proprietary rights of third parties. The Group may become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to its products and technology. Third parties may assert infringement claims against the Group based on existing patents or patents that may be granted in the future or other intellectual property rights. Although no such claims have been asserted against the Group to date, there can be no assurance that such claims will not be asserted in the future. If the Group is found to infringe a third party's intellectual property rights, it could be required to obtain a licence from such third party to continue developing and commercialising the relevant products and technology. However, it may not be able to obtain any required licence on commercially reasonable terms, or at all. Even if it is able to obtain a licence, it may be non-exclusive, thereby giving competitors access to the same products and technologies. Alternatively, the Group could be forced, including by court order, to cease commercialising the infringing technology or product. In addition, in any such proceeding or litigation, the Group could be found liable for monetary damages. A finding of infringement could prevent the Group from commercialising its product candidates or force it to cease some of its business operations, which could materially adversely affect its business and prospects. Any successful claims by third parties that the Group has misappropriated their confidential information or trade secrets could have a similarly negative impact on the Group's business and prospects.

The Group may be subject to claims that its employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Most of the Group's employees, including senior management, were previously employed at other biotechnology or pharmaceutical companies and it is anticipated that the Group will continue to employ experienced personnel. Some of these employees, including the Executive Director and the Senior Managers, may have executed proprietary rights, non-disclosure and non-competition agreements in connection with

such previous employment. Although the Group tries to ensure that employees do not use the proprietary information or know-how of others in their work, the Group may be subject to claims that the Group or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of their former employers. If the Group fails in successfully defending any such claims as may arise, it may be obliged to pay monetary damages and may also lose valuable intellectual property rights or personnel.

Intellectual property disputes could cause the Group to spend substantial resources and distract personnel from normal operational responsibilities.

Even if resolved in the Group's favour, litigation or other legal proceedings relating to intellectual property claims may require the Group to incur significant expenses and could distract technical and/or management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and, if securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the Company's Share price. Such litigation or proceedings could substantially increase operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities and the Group may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Moreover, counterparties to any litigation may have greater financial resources than the Group and therefore be better able to sustain the costs of such litigation or proceedings.

Inability to protect the confidentiality of trade secrets could harm the Group's business and competitive position.

In addition to seeking patents for some of its technology and products, the Group also relies on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain its competitive position. The Group seeks to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as employees, corporate collaborators, third party scientific collaborators, contract manufacturers, consultants, advisors and other third parties. It also enters into confidentiality and invention or patent assignment agreements with its employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose proprietary information, including trade secrets, and the Group may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is often unpredictable. In addition, some courts both within and outside the US may be less willing or unwilling to protect trade secrets. Moreover, if any of the Group's trade secrets were to be lawfully obtained or independently developed by a competitor, the Group would have no right to prevent such competitor from using that technology or information to compete with it. The loss of any of its trade secrets could harm the Group's competitive position and, consequently, materially adversely affect its business, financial condition, results of operations and prospects.

RISKS RELATED TO INTERNAL CONTROL AND FINANCIAL INFORMATION

The Group's ability to compete and grow depends to a large extent upon the continued service of the current management team and the timely recruitment of the direct sales force.

The services of the Group's management team are critical to the successful implementation of its product development and regulatory strategies and its ability to compete and grow depends in a large part upon the continued service of the management team. The Group's management team, including in particular Mike Bolinder, the Group's CEO, Gary Gemignani, the Group's CFO, and Dr. Gabriel Fox, the Group's Chief Medical Officer, have significant experience in the development, marketing and commercialisation of pharmaceutical products. See Sections 1, 2 and 3 of Part VII (*Directors, Senior Managers and Corporate Governance*) of this Prospectus. Members of the Group's management team may terminate their employment with the Group at any time subject to the terms of their employment contracts, which have notice periods of zero (most US employees) to twelve months.

The loss of the services of one or more of the Group's management team and the inability to find and recruit suitable replacements in a timely manner could harm its ability to achieve the successful development or commercialisation of its product candidates, and consequently have a material adverse effect on the Group's business, financial condition, results of operations and prospects.

The Group currently intends to recruit an initial sales force of approximately 30 field sales representatives at launch together with a further 10 support and managerial staff. The Company plans to increase the sales force to approximately 60 representatives within 36 months of the launch of BARHEMSYS® and BYFAVO™, as demand for the products grows. The ability of the Group to expand will depend in part upon it successfully employing and maintaining such a sales force.

The Group has grown and will continue to need to grow rapidly and it may experience difficulties in managing this growth.

The Group has expanded from six full-time employees in March 2018 to 37 full-time employees at the date of this Prospectus, with the further addition of approximately 30 sales staff and 10 support staff planned to complete the sales and marketing organisation comprised of experienced sales, marketing, operations, regulatory and medical affairs employees targeted at the launch of BARHEMSYS® and BYFAVO™. The Group expects to experience further growth in the number of its employees and the scope of its operations in connection with commercialisation of its product candidates. This potential growth may place a significant strain on the Group's management, operations and financial resources, and the Group may have difficulty managing this future potential growth. As the Group's development and commercialisation plans and strategies develop, additional managerial, operational, sales, marketing, financial and other resources will be required.

Future growth would impose significant and increasing challenges on members of management, including:

- identifying, recruiting, maintaining, motivating and integrating additional employees;
- building and managing an effective sales and marketing team;
- improving managerial, development, operational and finance systems and expanding facilities; and
- managing internal development efforts effectively while complying with contractual obligations to licensors, licensees, contractors and other third parties.

As the Group's operations expand, it will need to manage the commercial supply of BARHEMSYS® and BYFAVO™, sales and marketing activities, licensing activities, development activities and hire, train and integrate additional management, administrative and sales and marketing personnel. It will also need to manage an increased number of relationships with various strategic partners, suppliers and other third parties. The failure to accomplish any of these tasks could adversely affect the Group's ability to commercialise its product candidates and successfully expand its business.

Inability to attract and retain highly qualified employees may limit the Group's growth and prospects.

Because of the specialised scientific, technical, commercial and managerial nature of the Group's business, the Group relies on its ability to attract, retain, manage and motivate qualified scientific, technical, commercial and managerial personnel with relevant experience in the development and commercialisation of pharmaceutical products. The competition for qualified personnel in the pharmaceutical field is intense and, as a result, the Group may be unable to continue to attract and retain qualified personnel necessary for the development of its business or to recruit suitable replacement personnel. The inability to hire or retain experienced personnel could inhibit the Group's ability to execute its business plan and materially adversely affect its business, financial condition, results of operations and prospects.

Employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could have a material adverse effect on the Group's business.

The Group is exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to: comply with pharmaceutical regulations, provide accurate information to regulatory authorities, comply with manufacturing standards, comply with national and international fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorised activities. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion activities, sales commissions, customer incentive programmes and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to the Group's reputation.

It is not always possible to identify and deter employee misconduct, and precautions taken to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting the Group from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. If any such actions are instituted against the Group, and it is not successful in defending itself or asserting its rights, those actions could have a material adverse effect on its business, financial condition, results of operations and prospects, including through the imposition of significant fines or other sanctions.

The Group's business and operations would suffer in the event of system failures at the Group or third parties on which the Group relies.

Despite the implementation of security measures, the Group's internal computer systems, and those of the contracted CROs and other third parties on which the Group relies, are vulnerable to damage from computer viruses, unauthorised access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in the Group's operations, it could result in a material disruption of its drug development programmes. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in regulatory approval efforts and significantly increase costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of, or damage to, Group data or applications, or inappropriate disclosure of confidential or proprietary information, the Group could incur liability and the further development of its product candidates could be delayed, which could materially adversely affect its business, financial condition, results of operations and prospects.

RISKS RELATED TO THE FUNDRAISING AND OWNERSHIP OF THE COMPANY'S ORDINARY SHARES

The price of the Company's Ordinary Shares may be volatile, and all or part of an investment could be lost.

The future trading price of the Company's Ordinary Shares may be subject to fluctuations in response to various factors, some of which are beyond the Group's control. In addition to the factors discussed in this Part II (*Risk Factors*) and elsewhere in this Prospectus, these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to the Group's products or competitors' products;
- actual or anticipated changes in the Group's growth rate relative to competitors;
- announcements by the Group or its competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- results of clinical trials of the Group's product candidates or those of competitors;
- regulatory or legal developments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any product candidates or clinical development programs;
- the results of the Group's efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in the Group's financial results or those of companies that are perceived to be similar to the Group's;
- fluctuations in the valuation of companies perceived by investors to be comparable to the Group's;
- share price and volume fluctuations attributable to inconsistent trading volume levels of the Ordinary Shares;
- announcement or expectation of additional financing efforts;
- sales of the Company's Ordinary Shares by the Company or significant Shareholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

In addition, the stock market in general, and shares of specialty pharmaceutical and biotechnology companies in particular, have experienced price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of the Company's share capital, regardless of actual operating performance. The realisation of any of the above risks or any of a broad range of other risks, including

those described in this Part II (*Risk Factors*), could have a dramatic and material adverse impact on the market price of the Ordinary Shares.

The Group does not anticipate paying any dividends in the foreseeable future and, therefore, investors will need to rely on capital appreciation, if any, for any return on their investment.

The Group has never declared or paid cash dividends on its Shares. The Group currently intends to retain all of its future earnings, if any, to finance the growth and development of its business. In addition, the terms of any future debt agreements may preclude it from paying dividends. As a result, capital appreciation, if any, of the Ordinary Shares will be the sole source of gain for investors for the foreseeable future.

Future sales and issuances of Ordinary Shares or rights to purchase Ordinary Shares, including pursuant to any equity incentive plans, could result in additional dilution of the percentage ownership of Shareholders and could cause the Ordinary Share price to fall.

To raise capital in the future, the Group may issue substantial amounts of Ordinary Shares or securities convertible into or exchangeable for Ordinary Shares. These future issuances of Ordinary Shares or share-related securities, together with the exercise of outstanding options, may result in material further dilution to investors and new investors could gain rights, preferences and privileges senior to those of holders of share capital. Following the issue of the New Ordinary Shares to be allotted pursuant to the Fundraising, Shareholders will suffer dilution of approximately 14.7 per cent to their proportionate ownership and voting rights in the Company immediately prior to the Fundraising. In addition, Shareholders will be diluted by the issue of Ordinary Shares to Cosmo in consideration of a milestone payment of €5 million due upon the first commercial sale of BYFAVO™ by the Operating Company, which is expected to be satisfied by the issue of New Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the first commercial sale of BYFAVO™ by the Operating Company. The number of Ordinary Shares to be issued to Cosmo is not known at the date of this document but, based on the closing price of the Ordinary Shares on the Latest Practicable Date of €2.70, the Company would be required to issue 1,851,852 Ordinary Shares to satisfy such milestone payment, resulting in a dilution to Shareholders' proportionate ownership and voting rights of approximately 2.48 per cent.

The market price of the Ordinary Shares could be negatively impacted by sales of substantial amounts of Ordinary Shares, in particular following the expiry of the relevant lock-up periods.

Cosmo, the Directors and the Senior Managers have each agreed not to sell or otherwise dispose of any Ordinary Shares or any interest therein for a certain period without the prior written consent of Jefferies and Guggenheim Securities. In addition, the Company has agreed not to issue any further Shares for a certain period without the prior written consent of Jefferies and Guggenheim Securities. Sales of a substantial number of Ordinary Shares by investors with large shareholdings in the Company after these restrictions expire, or the knowledge that any of them will, or the perception that these sales may occur, could depress the market price of the Ordinary Shares and could impair the Company's ability to raise capital through the sale of additional equity securities.

Shareholders may have difficulty in effecting service of process on the Company or the Directors in any territory outside the UK, including the US, in enforcing US or other international judgments in the UK or in enforcing US federal or other international securities laws in UK courts.

Certain Directors are residents of the UK or Europe and substantially all of their assets are in Europe and as such outside the US. The Company is incorporated outside the US and most of its assets are located outside the US. As a result, it may not be possible for Shareholders to effect service of process within the US upon all of the Directors or on the Company, or to obtain discovery of relevant documents and/or the testimony of witnesses in the US. US Shareholders may have difficulties enforcing in courts outside the US judgments obtained in US courts against some of the Directors or the Company (including actions under the civil liability provisions of the US federal securities laws). Shareholders may also have difficulty enforcing liabilities under the US federal securities laws in legal actions originally brought in jurisdictions located outside the US. Similar risks apply to Shareholders resident in other territories outside the UK.

Changes in tax legislation or the interpretation of tax legislation could affect the Company's ability to provide returns to Shareholders.

Any change in (or in the interpretation of) tax legislation could affect the Company's ability to provide returns to Shareholders. Statements in this document in relation to tax and concerning the taxation of investors in Ordinary Shares are based on current tax law and practice which is subject to change.

The taxation of an investment in the Company depends on the specific circumstances of the relevant investor. The nature and amount of tax which the Company is expected to pay and the reliefs expected to be available are each dependent upon a number of assumptions, any one of which may change and which would, if so changed, affect the nature and amount of tax payable and reliefs available. Any changes in tax law, interpretation or practice could increase the amount of tax payable by the Company.

*The Company is treated as a PFIC for the taxable year ending 31 December 2019 and the Company believes that that there is a significant likelihood that it will be classified as a passive foreign investment company ("***PFIC***"), for US federal income tax purposes for its current taxable year and may be so classified in future taxable years. Such classification could result in adverse US federal income tax consequences to US investors.*

As described in Section B of Part XIII (*Taxation*) of this Prospectus under the heading "Certain US Federal Income Tax Considerations", the Company is treated as a PFIC for the taxable year ending 31 December 2019 and the Company believes that there is a significant likelihood that it will be classified as a PFIC for its current taxable year and may be so classified in future taxable years. Unless a US shareholder makes one of the elections described under that sub-section "Certain US Federal Income Tax Considerations—Passive Foreign Investment Company Considerations", which may or may not be available (and the availability as to which the Company makes no representations), US persons who hold the Ordinary Shares may be subject to adverse US federal income tax consequences on certain distributions and any gain with respect to the Ordinary Shares. Prospective US shareholders of Ordinary Shares should consult their own US tax advisers regarding the potential application of the PFIC rules.

Any sale, purchase or exchange of Ordinary Shares may become subject to the Financial Transaction Tax.

On 14 February 2013, the EU Commission published a proposal for a Council Directive (the "**Draft Directive**") for a common financial transaction tax ("**FTT**") in Austria, Belgium, Estonia, France, Germany, Greece, Italy, Portugal, Spain, Slovakia and Slovenia. In December 2015, Estonia withdrew from the group of states willing to introduce the FTT (the "**Participating Member States**").

The Draft Directive has very broad scope and could, if introduced, apply to certain dealings in the Ordinary Shares (including secondary market transactions) in certain circumstances. Pursuant to the Draft Directive, the FTT would be payable on financial transactions, provided at least one party to the financial transaction was established or deemed established in a Participating Member State and there was a financial institution established or deemed established in a Participating Member State which was a party to the financial transaction, or was acting in the name of a party to the transaction.

However, the Draft Directive is still subject to negotiation among the Participating Member States and therefore may be changed at any time. Moreover, if the Draft Directive were to be adopted (the "**Directive**"), it would need to be implemented into the respective domestic laws of the Participating Member States and the domestic provisions implementing the Directive might deviate from the Directive itself.

In addition, in December 2019, the German Federal Minister of Finance presented his European counterparts with a first draft bill on the FTT. This draft bill initially provides for a tax on share purchases in ten EU Member States.

Investors should consult their own tax advisers in relation to the potential consequences of the FTT associated with subscribing for, purchasing, holding and disposing of the Ordinary Shares.

In the absence of legally binding agreement between the UK and the EU governing their future trade relationship by 31 December 2020, the UK's withdrawal from the European Union may affect the shared jurisdiction rules applicable to the Company under the Takeover Directive with the result that some of the protections currently offered to Shareholders under the City Code will cease to apply.

The Company is subject to the City Code and therefore its Shareholders are entitled to certain protections afforded by the City Code. As Acacia Pharma is a company with its registered office in England and Wales that is only admitted to trading on Euronext Brussels, the shared jurisdiction rules pursuant to article 4 of the Takeover Directive apply to any takeover bid for the company. Accordingly, any takeover bid would fall under the shared jurisdiction of the UK Takeover Panel and the Belgian FSMA, who would jointly regulate the takeover bid.

The City Code would apply to the takeover bid in respect of matters relating to the information to be provided to the employees of the Company and matters relating to UK company law (in particular, the percentage of voting rights which confers control and any derogation from the obligation to launch an offer, as well as the conditions under which the Board could undertake any action which might result in the

frustration of an offer) ("**employee information and company law matters**"). Such employee information and company law matters would be administered by the Takeover Panel. The Belgian Act of 1 April 2007 on takeover bids (the "**Belgian Takeover Act**") and the Belgian Royal Decree of 27 April 2007 on takeover bids (the "**Belgian Takeover Decree**" and together with the Belgian Takeover Act, the "**Belgian Takeover Laws**") would apply in relation to matters relating to the consideration offered in the context of a takeover bid (in particular the bid price per share) and matters relating to the offer procedure (in particular, the information on any bidder's decision to make a takeover bid, the contents of the relevant offer document or prospectus and the disclosure of the Takeover Bid) ("**consideration and procedural matters**"). Such consideration and procedural matters would be administered by the Belgian FSMA. The FSMA would approve the offer document or prospectus and such document or prospectus would not be subject to any other regulatory approval as the contents of such document are regulated by the Belgian Takeover Laws. Any takeover bid itself would be approved by the Belgian FSMA.

In the event that, on 31 December 2020, no legally binding agreement between the UK and the EU governing the future trade relationship has been reached, then the shared jurisdiction rules in section 3(a)(iii) of the Introduction to the City Code are likely to be deleted with effect from 11.00 p.m. on that date. As the Company is not currently considered by the Takeover Panel to have its place of central management and control in the United Kingdom, the City Code will cease to apply to any takeover bid for it with effect from this time (in the event that any takeover bid was at that time continuing) and thereafter will not apply to the Company for so long as its central management and control remains outside of the UK.

As an English public company limited by shares, certain capital structure decisions will require Shareholder approval, which may limit the Company's flexibility to manage its capital structure.

On 22 September 2015, the Company altered its legal status under English law from a private company limited by shares by re-registering as a public company limited by shares. Subject to certain exceptions, English law provides that a board of directors may only allot shares (or rights to subscribe for, or convert securities into, shares) with the prior authorisation of shareholders, such authorisation stating the aggregate nominal amount of shares that it covers and its date of expiry (up to a maximum period of five years), each as specified in the articles of association or relevant shareholder resolution. The Company has obtained authority from its Shareholders to allot additional Shares up to an aggregate nominal amount of £640,000, such authority to expire at the Company's annual general meeting to be held in 2021. Following the utilisation or expiry of this authority, the Company will be required to seek Shareholder authority before it can allot further Shares.

English law also generally provides shareholders with pre-emption rights when new shares are issued for cash. However, it is possible for the articles of association, or for shareholders to pass a special resolution at a general meeting, being a resolution passed by at least 75% of the votes cast, to disapply pre-emption rights. Such a disapplication of pre-emption rights may be for a maximum period of up to five years from the date of adoption of the articles of association, if the disapplication is contained in the articles of association, or from the date of the shareholder special resolution, if the disapplication is by shareholder special resolution. In either case, this disapplication would need to be renewed by shareholders upon its expiration (i.e. at least every five years). The Company has obtained authority from its Shareholders to disapply pre-emption rights in respect of the allotment of up to an aggregate nominal amount of £640,000, such authority to expire at the Company's annual general meeting to be held in 2021. Following the utilisation or expiry of this authority, the Company will be required to seek Shareholder authority before it can allot further Shares otherwise than on a pre-emptive basis.

English law also generally prohibits a public company from repurchasing its own shares without the prior approval of shareholders by ordinary resolution, being a resolution passed by a simple majority of votes cast, and other formalities. Such approval may be for a maximum period of up to five years. See Sections 4 and 5 of Part XIV (*Additional Information*) for further information about the Shares and a summary of the Company's articles of association.

The Company is an emerging growth company and its disclosure of only two-years of audited financial statements in this Prospectus may make its Shares less attractive to investors.

The Company is an emerging growth company as defined in Section 2(a)(19) of the US Securities Act of 1933, as amended. As an emerging growth company, it is providing more limited disclosure in this Prospectus than other public companies. The Company has provided only two years of audited financial statements in this Prospectus, in addition to the unaudited interim financial statements for the six months ended 30 June 2020, with corresponding "Operating and Financial Review" disclosure.

The Directors cannot predict whether investors will find the Shares less attractive if the Company provides more limited disclosure. If some investors find the Shares less attractive as a result, there may be a less active trading market for the Shares and the Share price may be more volatile.

PART III

DIRECTORS, COMPANY SECRETARY, REGISTERED OFFICE AND ADVISERS

Directors	Scott Byrd (Non-Executive Chairman) Mike Bolinder (Chief Executive Officer) Edward J. Borkowski (Non-Executive Director) Dr John Brown (Senior Independent Non-Executive Director) Alessandro Della Chà (Non-Executive Director)
Company Secretary	Anne-Marie Elsley
Registered office and Directors' business address	Acacia Pharma Group plc The Officers' Mess Royston Road, Duxford Cambridge CB22 4QH United Kingdom
Joint Bookrunners	Jefferies International Limited 100 Bishopsgate London EC2N 4JL United Kingdom Guggenheim Securities, LLC 330 Madison Avenue New York NY 10017 United States
Joint Bookrunner and Listing Agent	Bank Degroof Petercam SA/NV Rue de l'Industrie / Nijverheidsstraat 44 1040 Brussels Belgium
Legal advisers to the Company as to English law	Stephenson Harwood LLP 1 Finsbury Circus London EC2M 7SH United Kingdom
Legal advisers to the Banks as to US and English Law and to the Fundraising as to US law	White & Case LLP 5 Old Broad Street London EC2N 1DW United Kingdom
Auditor	PricewaterhouseCoopers LLP The Maurice Wilkes Building St John's Innovation Park Cowley Road Cambridge CB4 0DS United Kingdom
Registrar	Equiniti Limited Aspect House Spencer Road Lancing West Sussex BN99 6DA United Kingdom

PART IV

EXPECTED TIMETABLE OF PRINCIPAL EVENTS AND FUNDRAISING STATISTICS

EXPECTED TIMETABLE OF PRINCIPAL EVENTS [(1)(2)]

Event	Time and Date
	3:00 p.m. CET on
Announcement of the Fundraising	13 August 2020
Publication of the Prospectus	14 August 2020
Admission and commencement of unconditional dealings in New Ordinary Shares issued pursuant to the Fundraising on Euronext Brussels	8:00 a.m. CET on 18 August 2020
Delivery of the New Ordinary Shares issued pursuant to the Fundraising to investors' securities accounts	18 August 2020
Despatch of definitive share certificates for the New Ordinary Shares issued pursuant to the Fundraising (where applicable)	By 28 August 2020

Notes:

(1) The times and dates in the table above are indicative only and are subject to change without further notice. All times are Brussels times unless otherwise stated.

(2) No temporary documents of title will be issued

FUNDRAISING STATISTICS

Placing Price per New Ordinary Share	€2.00
Number of Existing Ordinary Shares in issue immediately prior to Admission[(1)(2)]	72,779,729
Number of New Ordinary Shares to be issued by the Company pursuant to the Fundraising	12,500,000
Enlarged Share Capital immediately following completion of the Fundraising[(1)]	85,279,729
New Ordinary Shares as a percentage of the Enlarged Share Capital[(1)]	14.7%
Estimated net proceeds of the Fundraising receivable by the Company[(3)] *(millions)*	€22.1
Expected market capitalisation of the Company immediately following completion of the Fundraising[(1)(4)] *(millions)*	€230.3
Ticker Symbol	ACPH
ISIN for the New Ordinary Shares	GB00BYWF9Y76
Company's LEI code	213800SLDKXWKT6E3381

Notes:

(1) Assumes that no other Ordinary Shares are issued or share options exercised following the date of this Prospectus prior to Admission.

(2) Excludes any New Ordinary Shares which are issued.

(3) Net proceeds receivable by the Company are stated after deduction of commissions and other expenses of approximately €22.1 million.

(4) Calculated using the closing price of the Ordinary Shares on the Latest Practicable Date, The market capitalisation of the Company at any given time will depend on the market price of the Ordinary Shares at that time. There can be no assurance that the market price of an Ordinary Share will equal or exceed the Placing Price.

PART V

PRESENTATION OF INFORMATION

1. Notice to prospective investors

Prospective investors should rely only on the information in this Prospectus when deciding whether to invest in the New Ordinary Shares. No person has been authorised to give any information or to make any representations in connection with the Fundraising other than those contained in this Prospectus and, if given or made, such information or representation must not be relied upon as having been authorised by or on behalf of the Company, the Directors or any of the Banks. No representation or warranty, express or implied, is made by any of the Banks or any selling agent as to the accuracy or completeness of such information, and nothing contained in this Prospectus is, or shall be relied upon as, a promise or representation by any of the Banks or any selling agent as to the past, present or future. Without prejudice to any obligation of the Company to publish a supplementary prospectus pursuant to section 87G of FSMA and paragraph 3.4.1 of the Prospectus Regulation Rules, neither the delivery of this Prospectus nor any issue or sale of the New Ordinary Shares pursuant to the Fundraising made under this Prospectus shall, under any circumstances, create any implication that there has been no change in the business or affairs of the Company or of the Group taken as a whole since the date hereof or that the information contained herein is correct as of any time subsequent to the earlier of the date hereof and any earlier specified date with respect to such information.

The Company will update the information provided in this Prospectus by means of a supplement hereto if a significant new factor, material mistake or inaccuracy relating to this Prospectus occurs or arises prior to Admission that may affect the ability of prospective investors to make an informed assessment of the Fundraising. The Prospectus and any supplement thereto will be subject to approval by the FCA and will be made public in accordance with the Prospectus Regulation Rules. If a supplement to the Prospectus is published prior to Admission, investors shall have the right to withdraw their subscriptions made prior to the publication of such supplement. Such withdrawal must be done within the time limits set out in the supplement (if any) (which shall not be shorter than two clear business days after publication of such supplement).

The contents of this Prospectus are not to be construed as legal, financial, business or tax advice. Each prospective investor should consult its own lawyer, financial adviser or tax adviser for legal, financial or tax advice in relation to any purchase or proposed purchase of the New Ordinary Shares. Each prospective investor should consult with such advisers as needed to make its investment decision and to determine whether it is legally permitted to hold New Ordinary Shares under applicable legal, investment or similar laws or regulations. Investors should be aware that they may be required to bear the financial risks of any investment in New Ordinary Shares for an indefinite period of time.

This Prospectus is not intended to provide the basis of any credit or other evaluation and should not be considered as a recommendation by any of the Company, the Directors, the Banks or any of their respective representatives that any recipient of this Prospectus should subscribe for or purchase the New Ordinary Shares.

Prior to making any decision whether to purchase any New Ordinary Shares, prospective investors should ensure that they have read this Prospectus in its entirety and, in particular, Part II (*Risk Factors*), and not just rely on key information or information summarised in it. In making an investment decision, prospective investors must rely upon their own examination of the Company and the terms of this Prospectus, including the merits and risks involved. Any decision to purchase New Ordinary Shares should be based solely on this Prospectus.

Investors who purchase New Ordinary Shares pursuant to the Fundraising will be deemed to have acknowledged that:

(i) they have not relied on either of the Banks or any person affiliated with either of them in connection with any investigation of the accuracy of any information contained in this Prospectus or their investment decision;

(ii) they have relied solely on the information contained in this Prospectus; and

(iii) no person has been authorised to give any information or to make any representation concerning the Group or the New Ordinary Shares (other than as contained in this Prospectus) and, if given or made, any such other information or representation should not be relied upon as having been authorised by any of the Company, the Directors or the Banks.

None of the Company, the Directors or the Banks or any of their representatives is making any representation to any offeree or purchaser of the New Ordinary Shares regarding the legality of an investment by such offeree or purchaser.

Apart from the responsibilities and liabilities, if any, which may be imposed on the Banks by any of the FCA, the National Bank of Belgium or the Belgian FSMA, or the regulatory regimes established thereunder or under the regulatory regime of any jurisdiction where the exclusion of liability under the relevant regime would be illegal, void or unenforceable, none of the Banks accepts any responsibility whatsoever, and makes no representation or warranty, express or implied, for the contents of this Prospectus, including its accuracy, completeness or for any other statement made or purported to be made by it or on behalf of it, the Company, the Directors or any other person, in connection with the Company, the New Ordinary Shares or the Fundraising and nothing in this Prospectus shall be relied upon as a promise or representation in this respect, whether as to the past or the future. Each of the Banks accordingly disclaims all and any liability whatsoever, whether arising in tort, contract or otherwise (save as referred to above), which it might otherwise have in respect of this Prospectus or any such statement.

In connection with the Fundraising, each of the Banks and any of their respective affiliates, acting as an investor for its or their own account(s), may acquire New Ordinary Shares, and in that capacity may retain, purchase, sell, offer to sell or otherwise deal for its or their own account(s) in New Ordinary Shares and other securities of the Company or related investments in connection with the Fundraising or otherwise. Accordingly, references in this Prospectus to the New Ordinary Shares being offered, acquired, placed or otherwise dealt in should be read as including any issue or offer to, or subscription, acquisition, dealing or placing by, each of the Banks and any of their respective affiliates acting as an investor for its or their own account(s). None of the Banks intends to disclose the extent of any such investment or transactions otherwise than in accordance with any legal or regulatory obligations to do so. In addition, in connection with the Fundraising, any of the Banks may enter into financing arrangements with investors, such as share swap arrangements or lending arrangements where New Ordinary Shares are used as collateral, which could result in such Banks acquiring shareholdings in the Company.

The Banks and their respective affiliates may have engaged in transactions with, and provided various investment banking, financial advisory and other services to, the Company for which they would have received customary fees. The Banks and any of their respective affiliates may provide such services to the Company and any of its affiliates in the future.

2. Presentation of financial information

Unless otherwise indicated, the financial information included in this document is prepared in accordance with International Financial Reporting Standards and International Financial Reporting Standards Interpretations Committee interpretations as adopted by the European Union ("**IFRS**"), and those parts of the Companies Act applicable to the companies reporting under IFRS. IFRS, as adopted by the European Union, differs in certain aspects from International Financial Reporting Standards as issued by the International Accounting Standards Board.

The preparation of financial information in conformity with IFRS requires the use of certain critical accounting estimates. Further details are set out in Section 12 (*Critical accounting policies*) of Part X (*Operating and Financial Review*) of this Prospectus. It also requires management to exercise its judgment in the process of applying the Company's accounting policies. The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the financial information are disclosed in the notes to the financial information set out in the 2018 Annual Financial Statements, the 2019 Annual Financial Statements and the 2020 Interim Financial Statements which are referred to in Part XI (*Historical Financial Information*).

The Company's financial year runs from 1 January to 31 December. The financial information included in this Prospectus is not intended to comply with the applicable accounting requirements of the Securities Act and the related rules and regulations that would apply if the New Ordinary Shares were to be registered in the US. Compliance with such requirements would require the modification or exclusion of certain information included in this Prospectus and the presentation of certain information which is not included in this Prospectus.

Financial information presented in this Prospectus for the financial year ended 31 December 2018 remains in pounds sterling and is derived from the audited financial statements for the year ended 31 December 2018 incorporated by reference in this Prospectus. Unaudited financial information presented in this Prospectus for the financial year ended 31 December 2018 in US dollars is derived from the unaudited comparative presented in the financial statements for the year ended 31 December 2019 incorporated by reference in this

Prospectus. Financial information presented in this Prospectus for the financial year ended 31 December 2019 remains in US dollars and is derived from the audited financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus.

The financial information presented in this document was not prepared in accordance with US Generally Accepted Accounting Principles ("**US GAAP**") or audited in accordance with US Generally Accepted Auditing Standards ("**US GAAS**") or the standards of the Public Company Accounting Oversight Board ("**PCAOB Standards**"). No opinion or any other assurance with regard to any financial information was expressed under US GAAS or PCAOB Standards and the financial information is not intended to comply with SEC reporting requirements. Compliance with such requirements would require the modification, reformulation or exclusion of certain financial measures. In addition, changes would be required in the presentation of certain other information. In particular, no reconciliation to US GAAP is provided.

3. **Market, economic and industry data**

This Prospectus includes market share, industry and scientific data and forecasts that the Company has obtained from industry publications, surveys and internal Company sources. As noted in this Prospectus, the Company has obtained market data relating to the Group's business from providers, including:

- Bridgehead International Ltd. ("**Bridgehead**") (e.g. Acacia Pharma Market Research, Bridgehead, March 2008);
- Life Science Strategy Group LLC ("**LSSG**") (e.g. Acacia Pharma Market Research, LSSG, November 2014);
- Link Group for Cosmo Technologies (March 2019);
- LSSG 2016;
- Icon Group International Inc. ("**ICON**") (e.g. Acacia Pharma Market Research, ICON, November 2014);
- National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006; Source Healthcare;
- World Cancer Research Fund International, http://www.wcrf.org/int/cancer-facts-figures/worldwide-data (19/8/15); and
- Acacia Pharma Preliminary US BARHEMSYS® Sales and Marketing Plan, October 2019;
- Symphony Health, Source Non Retail, August 2017 – July 2018; and
- TwoLabs, MKO Global Partners Prepared for Cosmo Pharmaceuticals, 2018.

Publications

This Prospectus includes scientific data from the following publications:

- American Medical Association, Top 10 Opthalmic Procedures in Surgery Centers by Volume (2011).
- American Society of Plastic Surgeons, 2018 Plastic Surgery Statistics Report (2018).
- Apfel CC, Läärä E, Koivuranta M, et al. (1999). A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology 91(3): 693-700.
- Apfel CC, Korttila K, Abdalla M, et al. (2004). A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 350(24): 2441-2451.
- Apfelbaum JL, Gross JB, et al. (2018). Practice guidelines for moderate procedural sedation and analgesia 2018. Anesthesiology V 128(3):437-479.
- ASPE (Office of the Assistant Secretary for Planning and Evaluation, US Department of Health and Human Services) Issue Brief, June 2014.
- Basch E, Prestrud AA, Hesketh PJ, et al. (2011). Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 29(31): 4189-4198.
- Berger MH, Ettinger DS, et al. (2017). NCCN Guidelines® Insights: Antiemesis, Version 2.2017. J Nati Compr Canc Netw 15(7): 883-893.
- Canal M, Espie P and Thenot JP (2002). Amisulpride: Metabolic and pharmacokinetic profile after 14C intravenous administration. Eur Neuropsychopharmacol 12 (Supplement 3): 310-310.

- Candiotti KA, Kranke P, Bergese SD, et al (2019). Randomized, Double-Blind, Placebo-Controlled Study of Intravenous Amisulpride as Treatment of Established Postoperative Nausea and Vomiting in Patients Who Have Had No Prior Prophylaxis. Anesth Analg 128(6):1098-1105.
- Candrilli S and Mauskopf J (2006). How Much Does a Hospital Day Cost? 11th Annual International Meeting of ISPOR. Philadelphia, PA.
- Chang P, Okamoto M, Chen J, et al. (2005). Cost-effectiveness analysis of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting. J Manag Care Pharm 11(4): 317-321.
- Coulouvrat C and Dondey-Nouvel L (1999). Safety of amisulpride (Solian): a review of 11 clinical studies. Int Clin Psychopharmacol 14(4): 209-218.
- Edison analyst note on Tesaro, Deutsche Bank Securities Inc., February 2013.
- Edison analyst note on Tesaro, February 2014.
- Ferlay, J, et al (2018). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods.
- Fortney JT, Gan TJ, Graczyk S, et al. (1998). A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. S3A-409 and S3A-410 Study Groups. AnesthAnalg 86(4): 731-738.
- Fox GM, Albayaty M, et al. (2019). Intravenous amisulpride does not meaningfully prolong the QTc interval at doses effective for the management of postoperative nausea and vomiting. International Anesthesia Research Society.
- Fox GM, Roffel AF, et al. (2019). Metabolism and excretion of intravenous, radio-labeled amisulpride in healthy, adult volunteers. Clin Pharmacol: Advances and Applications 11: 161-169.
- Gan TJ, Meyer TA, Apfel CC, et al. (2007). Society for Ambulatory Anesthesia guidelines for the management of postoperative nausea and vomiting. AnesthAnalg 105(6): 1615-1628.
- Gan TJ, Diemunsch P, Habib AS, et al. (2014). Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 118(1): 85-113.
- Gan TJ, Belani KG, Bergese SD, et al. (2020). Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesth Analg doi: 10.1213/ANE.0000000000004833.
- Gan TJ, Kranke P, Minkowitz HS, et al. (2017). Intravenous Amisulpride for the Prevention of Postoperative Nausea and Vomiting: Two Concurrent, Randomized, Double-blind, Placebo-controlled Trials. Anesthesiology 126(2): 268-275.
- Glass PS, Everett L, Redmond M, et al. (2013). Optimal PONV Management – SCOR Database. ASA Annual Meeting. San Francisco, CA.
- Habib A, Curr Med Res Opin 2006; 22(6): 1093-1099.
- Habib AS and Gan TJ (2008). The use of droperidol before and after the Food and Drug Administration black box warning: a survey of the members of the Society of Ambulatory Anesthesia. JClinAnesth 20(1): 35-39.
- Habib AS, et al. (2019). Amisulpride for the Rescue Treatment of Postoperative Nausea or Vomiting in Patients Failing Prophylaxis – A Randomized, Placebo-controlled Phase III Trial Anesthesiology 2019, 130:203-212.
- Herrstedt J, Sigsgaard T, Handberg J, et al. (1997). Randomized, double-blind comparison of ondansetron versus ondansetron plus metopimazine as antiemetic prophylaxis during platinum-based chemotherapy in patients with cancer. JClinOncol 15(4): 1690-1696.
- Herrstedt J, Summers Y, Daugaard G, et al. (2017). Amisulpride in the prevention of nausea and vomiting induced by cisplatin-based chemotherapy: a dose-escalation study. Support Care Cancer doi 10.1007/s00520-017-3825-2.
- Herrstedt J, et al. (2018). Amisulpride prevents nausea and vomiting associated with highly emetogenic chemotherapy: a randomised, double-blind, placebo-controlled, dose-ranging trial Supportive Care in Cancer 2018, doi:10.1007/s00520-018-4564-8.

- Hesketh PJ, Grunberg SM, Gralla RJ, et al. (2003). The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin – the Aprepitant Protocol 052 Study Group. J Clin Oncol 21(22): 4112-4119.
- iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019.
- iData Research, US Market Procedure Numbers for Bronchoscopy October 2019.
- Jefferies International Limited analyst note, 19 March 2015.
- Joseph DA, Meester RGS, et al. (2016). Colorectal cancer screening: estimated future colonoscopy need and current volume and capacity. Cancer. 122(16): 2479-2486.
- Kaiser Family Foundation http://kff.org/other/state-indicator/expenses-per-inpatient-day/ (accessed 20 March 2020).
- Kantar Health. Payer Mix in Oncology: Understanding cancer pay mix is critical to understanding patient affordability as a component of launch planning.
- Koivuranta M, Läärä E, Snare L, et al. (1997). A survey of postoperative nausea and vomiting. Anaesthesia 52(5): 443-449.
- Kranke P, Eberhart L, Motsch J, et al. (2013). I.V. APD421 (amisulpride) prevents postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled, multicentre trial. Br J Anaesth 111(6): 938-945.
- Kranke P, Bergese S, Minkowitz H, et al. (2018). Amisulpride Prevents Postoperative Nausea and Vomiting in Patients at High Risk: A Randomized, Double-blind, Placebo-controlled Trial. Anesthesiology 128(6): 1099-1106.
- Macario A, Weinger M, Carney S, et al. (1999). Which clinical anesthesia outcomes are important to avoid? The perspective of patients. Anesth Analg 89(3): 652-658.
- MHRA: UK Pharmaceutical Assessment Report for amisulpride tablets, 2010.
- Morgan Stanley analyst note on Tesaro, 2012.
- Navari RM, Qin R, Ruddy KJ, et al. (2016). Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting. N Engl J Med 375(2): 134-142.
- Pastis NJ, et al. (2019). Safety and Efficacy of Remimazolam Compared With Placebo and Midazolam for Moderate Sedation During Bronchoscopy. Chest 155(1):137-146.
- Pizzi LT, Toner R, Foley K, et al. (2012). Relationship between potential opioid-related adverse effects and hospital length of stay in patients receiving opioids after orthopedic surgery. Pharmacotherapy 32(6): 502-514.
- Poli-Bigelli S, Rodrigues-Pereira J, Carides AD, et al. (2003). Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, double-blind, placebo-controlled trial in Latin America. Cancer 97(12): 3090-3098.
- Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019).
- Rapoport BL, Chasen MR, Gridelli C, et al. (2015). Safety and efficacy of rolapitant for prevention of chemotherapy-induced nausea and vomiting after administration of cisplatin-based highly emetogenic chemotherapy in patients with cancer: two randomised, active-controlled, double-blind, phase 3 trials. Lancet Oncol 16(9): 1079-1089.
- Rex DK, et al, (2018). A phase III study evaluating the efficacy and safety of remimazolam (CNS 7056) compared with placebo and midazolam in patients undergoing colonoscopy. Gastrointest Endosc. 2018. 88(3):427-437.
- Roila F, Molassiotis A, Herrstedt J, et al. (2016). 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. Ann Oncol 27(suppl 5): v119-v133.
- Taubel J, Ferber G, Fox G, et al. (2017). Thorough QT study of the effect of intravenous amisulpride on QTc interval in Caucasian and Japanese healthy subjects. Br J Clin Pharmacol 83(2): 339-348.

- The Lancet: Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes.
- Warr DG, Hesketh PJ, Gralla RJ, et al. (2005). Efficacy and tolerability of aprepitant for the prevention of chemotherapy-induced nausea and vomiting in patients with breast cancer after moderately emetogenic chemotherapy. J Clin Oncol 23(12): 2822-2830.
- Zeidenberg, Jerry (2007). Report on Interventional Radiology.

Third Party Reports

All sources referenced in this Prospectus are publicly available or historically commissioned reports, and are not expert reports for the purposes of the Prospectus Regulation Rules. The Company has not independently verified any of the data from third party sources nor has it ascertained the underlying economic assumptions relied upon therein. Statements or estimates as to the Group's market position, which are not attributed to independent sources, are based on market data or internal information currently available to the Company. The Company confirms that information sourced from third parties has been accurately reproduced and, as far as the Company is aware and is able to ascertain from information published from third parties, no facts have been omitted which would render the reproduced information inaccurate or misleading. Estimates extrapolated from this data involve risks and uncertainties and are subject to change based on various factors, including those discussed in Part II (*Risk Factors*).

Reliance on Third Party Data

The Director's estimates of the Group's market position and the size of its addressable market, for instance, rely on market share, industry and scientific data. To estimate its market position and the size of its addressable market the Group relies on certain assumptions and estimates of the number of procedures in which the Company's products could be used based on data on the number of surgeries or other procedures conducted. Some of this information is obtained from third party publications and surveys that are not updated regularly, resulting in the Group relying on information released over five years, and in some cases ten years, prior to the date of this Prospectus. The Company confirms that such estimates have been calculated based on such information as published by third party sources. Estimates relying on such data involve risks and uncertainties, see Part II (*Risk Factors*) "*The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs*."

4. **Rounding**

Certain numerical figures contained in this Prospectus, including financial information, market data and certain operating data, such as the number of clinical hospital procedures and clinical results, have been subject to rounding adjustments for ease of presentation. Accordingly, in certain instances, the sum of the numbers in a column or a row in tables may not conform exactly to the total figure given for that column or row or the sum of certain numbers presented as a percentage may not conform exactly to the total percentage given.

5. **Currencies**

Unless otherwise indicated in this Prospectus, all references to:

(a) "pounds sterling" or "£" are to the lawful currency of the UK;

(b) "$" or "US dollars" or "US$" are to the lawful currency of the US; and

(c) "Euros" or "€" are to the lawful currency of the European Union (as adopted by certain Member States).

Unless otherwise indicated, the financial information contained in this Prospectus has been expressed in US dollars. With effect from 1 January 2019, the Company changed its presentational currency from pounds sterling to US dollars and the Group has presented its consolidated financial statements in US dollars since that time. Where financial information has been converted from one currency to another, the relevant exchange rate used for such conversion is indicated based on the exchange rate information set out on page 93 of this document.

6. **Interpretation**

Certain terms used in this Prospectus, including capitalised terms, are defined in Part XV (*Definitions*) and Part XVI (*Glossary*).

All references to legislation in this Prospectus are to the legislation of England and Wales unless the contrary is indicated. Any reference to any provision of any legislation or regulation shall include any amendment, modification, re-enactment or extension thereof.

References to the singular in this Prospectus shall include the plural and vice versa, and words importing the masculine gender shall include the feminine or neutral gender where the context requires.

7. Forward-looking statements

Certain information contained in this Prospectus, including any information as to the Group's strategy, plans or future financial or operating performance, constitutes "forward-looking statements". These forward-looking statements may be identified by the use of forward-looking terminology, including the terms "believes", "estimates", "anticipates", "projects", "expects", "intends", "aims", "plans", "predicts", "may", "will", "seeks" or "should" or, in each case, their negative or other variations or comparable terminology, or by discussions of strategy, plans, objectives, goals, future events or intentions. These forward-looking statements include all matters that are not historical facts. They appear in a number of places throughout this Prospectus and include statements regarding the intentions, beliefs or current expectations of the Directors concerning, among other things, the Group's results of operations, financial condition, prospects, growth, strategies and the industry in which the Group operates.

Many factors may cause the Group's results of operations, financial condition and the development of the industries in which it competes to differ materially from those expressed or implied by the forward-looking statements contained in this Prospectus.

Prospective investors are advised to read, in particular, the following parts of this Prospectus for a more complete discussion of the factors that could affect the Group's future performance and the industry in which the Group operates: Part II (*Risk Factors*), Part VI (*Information on the Company and the Group*), Part X (*Operating and Financial Review*) and Part XI (*Historical Financial Information*). In light of these risks, uncertainties and assumptions, the events described in the forward-looking statements in this Prospectus may not occur.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future or are beyond the Group's control. Forward-looking statements are not guarantees of future performance. Even if the Group's actual results of operations, financial condition and the development of the industries in which the Group operates are consistent with the forward-looking statements contained in this Prospectus, those results or developments may not be indicative of results or developments in subsequent periods.

The forward-looking statements contained in this Prospectus speak only as of the date of this Prospectus. The Company, the Directors and the Banks expressly disclaim any obligation or undertaking to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required to do so by applicable law, the Prospectus Regulation Rules, the Disclosure Guidance and Transparency Rules or the EU Market Abuse Regulation (596/2014).

8. Enforcement of civil liabilities

Certain Directors are residents of the UK and Europe and substantially all of their assets are in Europe and as such outside the US. The Company is incorporated outside the US and many of its assets are located outside the US. As a result, it may not be possible for Shareholders to effect service of process within the US upon all of the Directors or on the Company, or to obtain discovery of relevant documents and/or the testimony of witnesses in the US. US Shareholders may have difficulties enforcing in courts outside the US judgments obtained in US courts against some of the Directors or the Company (including actions under the civil liability provisions of the US federal securities laws). Shareholders may also have difficulty enforcing liabilities under the US federal securities laws in legal actions originally brought in jurisdictions located outside the US. Similar risks apply to Shareholders resident in other territories outside the UK.

9. No incorporation of website information

The contents of the Company's or the Group's websites or any website directly or indirectly linked to the Company's or the Group's websites do not form part of this Prospectus and investors should not rely on them, save for those webpages specifically referred to in Part XI (*Historical Financial Information*) of this document.

PART VI

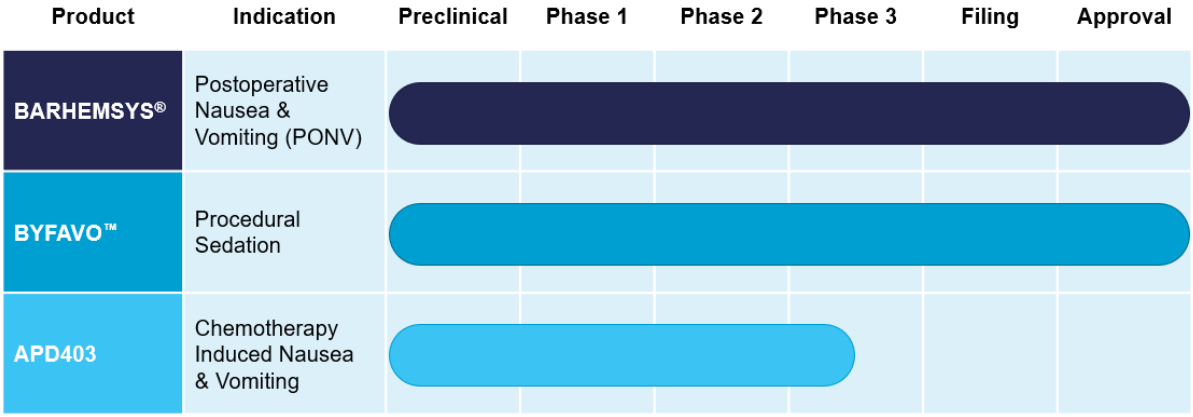
INFORMATION ON THE COMPANY AND THE GROUP

1. Business Overview

Acacia Pharma is a commercial stage biopharmaceutical company focused on developing and commercialising novel products to improve the care of patients undergoing serious medical treatments such as surgery, invasive procedures, or chemotherapy.

The Group's portfolio includes two FDA-approved products: BARHEMSYS®, a dopamine antagonist which has been developed for the prevention and treatment of post-operative nausea and vomiting (PONV), and BYFAVO™, a rapid onset/offset intravenous benzodiazepine sedative for use during certain invasive medical procedures in adult patients. In addition, the Group is developing an additional antiemetic product candidate, APD403, for chemotherapy-induced nausea and vomiting (CINV). The Group plans to launch both BARHEMSYS® and BYFAVO™ commercially in the US in the second half of 2020.

The following table summarises the Group's products and key programmes:



The Group's product pipeline is targeted to address significant unmet medical needs in commercially attractive markets. The Directors estimate that approximately 65 million invasive surgical procedures are undertaken per year in the US and antiemetic prophylaxis is used in approximately 49 million of such procedures.[1] The Directors further estimate that approximately 18 million patients who are deemed higher-risk are eligible for combination prophylaxis and 16 million patients require PONV rescue treatment upon the failure of prophylaxis[2], and these are the target markets for BARHEMSYS®. The number of surgical procedures annually worldwide is estimated at greater than 230 million[3]; the majority in the areas of general, orthopaedic/trauma and obstetric/gynaecological surgery. BYFAVO™ is approved by the FDA for use in invasive medical procedures in adult patients lasting 30 minutes or less, such as colonoscopy and bronchoscopy. The Directors estimate there are 25 million GI procedures annually in the US.[4]

Based on the above, the Directors estimate that the total addressable market in PONV rescue is $2.6 billion per year, calculated on the assumption that 16 million patients require PONV rescue treatment and using a selling price of $80 per 10 mg rescue dose with, on average, 2 rescue doses per patient. The secondary market in combination prophylaxis in highest risk patients is estimated at $720 million per year, calculated

---

[1] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005. Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

[2] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005; Life Science Strategy Group, LLC Market Research; Apfel et al.,2004. Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

[3] The Lancet: Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes.

[4] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

on the assumption that 18 million patients are deemed higher risk and using a selling price of $40 per 5 mg prophylaxis dose. The procedural sedation market is estimated by the Directors at over $1 billion per year, based on a selling price of $25 to $35 per dose with over 40 million procedures estimated to be undertaken per year.

The Group was founded in 2007 and is based in Cambridge, UK with US operations based in Indianapolis, Indiana. The Group has financed its operations and development activities to-date through a combination of support from strategic and specialist investors, partnerships and other debt and equity financing, including through its initial public offering on Euronext Brussels in in March 2018. Specifically, the Group has raised £43.0 million of private shareholder equity, primarily from Lundbeckfond, Novo, F-Prime and Gilde, and €38.1 million from the proceeds of its IPO (net of expenses). In June 2018, the Group secured and drew down $10 million pursuant to a term loan facility with Hercules Capital. This year, in connection with the BYFAVO™ Acquisition, the Group has secured new equity investments from Cosmo totalling €20 million, together with up to €25 million in debt financing that became available on the FDA approval of BYFAVO™, of which €15 million has been drawn down and €10 million is available for drawdown until 30 September 2020. Since its inception, the Group has also benefited from the receipt of £9.8 million in R&D tax credits.

1.1 *BARHEMSYS® (amisulpride)*

BARHEMSYS®, based on the active ingredient amisulpride, has been developed for the management of PONV, including for: (i) the rescue treatment of patients who suffer PONV despite having received prior prophylaxis with other antiemetics; and (ii) the prophylaxis of PONV, especially in combination with other antiemetics in higher risk patients. Amisulpride is a selective dopamine-2 (D2) and dopamine-3 (D3) receptor antagonist. Amisulpride, the active ingredient within BARHEMSYS®, is marketed in certain countries outside the US for the management of schizophrenia and other psychoses. The Group repurposed amisulpride for the management of nausea and vomiting and differentiated it by applying a change in route of administration and dose that is appropriate for the new use of BARHEMSYS®.

The FDA approved the NDA for BARHEMSYS® on 26 February 2020 and the Company is planning to launch BARHEMSYS® in the US in the second half of 2020 for the treatment of PONV. The Group is building specialist-focused sales and marketing capabilities in the US with the aim to initially target the promotion of BARHEMSYS® to hospital-based anaesthetists and their surgical teams for rescue treatment of PONV and subsequently promote earlier in the treatment pathway for the combination prophylaxis of PONV in higher-risk patients. While the Group has retained all rights to commercialise BARHEMSYS® in all territories and plans to commercialise it directly in the US, it may in the future seek to establish licensing and/or distribution agreements with selected pharmaceutical partners outside the US, where commercially viable and regulatory approvals are obtained and for which any necessary consents are obtained.

Core patents covering BARHEMSYS® have been granted to the Group in most major pharmaceutical territories, and additional patent applications are pending. For further information on the Group's patent position and other intellectual property rights see Section 9 of this Part VI (*Information on the Company and the Group*).

1.2 *BYFAVO™ (remimazolam)*

BYFAVO™, based on the active ingredient remimazolam, is a rapid onset/offset intravenous benzodiazepine sedative recently approved by the FDA for use during invasive medical procedures in adult patients lasting 30 minutes or less, such as during colonoscopy and bronchoscopy. In the human body, remimazolam is rapidly metabolised to an inactive metabolite by tissue esterases and is not metabolised by cytochrome-dependent hepatic pathways. Like other benzodiazepines, the effect of remimazolam can be reversed with flumazenil to rapidly terminate sedation or anesthesia if necessary. During clinical studies involving approximately 2,400 volunteers and patients, remimazolam demonstrated both efficacy and safety.

The FDA approved the NDA for BYFAVO™ on 2 July 2020 for procedural sedation in adults undergoing procedures lasting less than 30 minutes and, subject to completion of scheduling under the Controlled Substances Act by the Drug Enforcement Administration ("**DEA**"), which is expected in the coming weeks or months, the Company is planning to launch BYFAVO™ in the US in the second half of 2020. At the date of this Prospectus, the Company is not aware of any reason why scheduling under the Controlled Substances Act will not occur.

The licencing rights to BYFAVO™ are owned by Paion UK Limited ("**Paion**"), a wholly-owned subsidiary of Paion AG, a publicly-listed specialty pharmaceutical company headquartered in Aachen, Germany, which

completed the clinical development of BYFAVO™ for procedural sedation in colonoscopy and bronchoscopy in the US. The Group originally acquired the rights to develop and commercialise BYFAVO™ in the US from Cosmo, a specialty pharmaceutical company headquartered in Ireland, through a sub-licensing agreement in January 2020. With effect from 7 August 2020, Cosmo assigned its licence from Paion to develop and commercialise BYFAVO™ directly to the Company. Further details of the BYFAVO™ Sub-Licence and BYFAVO™ Assignment Agreement are set out in Section 18.4 of Part XIV (*Additional Information*) of this document.

The Directors believe BYFAVO™ can be promoted and commercialised through the same commercial organisation as is planned to be established for BARHEMSYS® with limited marginal marketing and regulatory costs that are specific to BYFAVO™.

In addition to procedural sedation, there are other possible attractive indications for further development in the US, including general anaesthesia (for which remimazolam is already approved in Japan) and ICU sedation beyond 24 hours.

There are a number of issued patents for BYFAVO™ and additional patent applications are pending. For further information on the Group's patent position and other intellectual property rights see Section 9 of this Part VI (*Information on the Company and the Group*).

1.3 *APD403 (amisulpride)*

APD403, based on the active ingredient amisulpride, is being developed for chemotherapy-induced nausea and vomiting (CINV), in particular for the management of delayed nausea in the two to five days following chemotherapy. Phase 2 clinical proof of concept studies have demonstrated safety and efficacy for APD403 in the management of CINV. The Company held a Type C meeting with the FDA in April 2019 at which it was confirmed that one of the Phase 2 studies already completed could potentially be acceptable to support the approval of APD403 and therefore that only one further, positive, pivotal clinical trial may now be required to support registration in CINV.

The Group has retained all rights to commercialise APD403 in all territories and plans to commercialise it directly in the US and to establish licensing and/or distribution agreements with selected pharmaceutical partners outside the US, where commercially viable and regulatory approvals are obtained and for which any necessary consents are obtained. The Directors believe that once BARHEMSYS® has been established in the US market, the existing sales and marketing infrastructure could be further moderately increased in size to commercialise APD403 for CINV, targeting hospital and clinic-based oncologists.

Core patents covering APD403 have been granted to the Group in most major pharmaceutical territories, and additional patent applications are pending.

2. Key Strengths

The Directors believe that the Group has the following key strengths:

2.1 *Focus on PONV and procedural sedation: large market opportunities with significant unmet medical needs*

The Group plans to launch BARHEMSYS® to address the post-operative care market. The Directors estimate that approximately 65 million antiemetic eligible surgical procedures are conducted each year in the US.[5] BARHEMSYS® represents an opportunity to improve patient care in such surgical procedures whilst offering hospitals opportunities to both reduce costs and improve reimbursement. Appropriate management of PONV is a key to improving patient satisfaction by reducing the side effects of surgery and also reducing the time patients spend in expensive recovery rooms and in-patient hospital beds. Moreover, US hospitals are financially incentivised to improve the quality of care, as well as reduce post-surgical patient recovery times and morbidity. BARHEMSYS® has been specifically developed to meet the key unmet needs within the management of PONV and is currently the only FDA-approved product specifically indicated for PONV rescue.

[5] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005. Please refer to Part II (*Risk Factors*) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

The Group plans to launch BYFAVO™ for use in the procedural sedation and anaesthesia market. The number of surgical procedures worldwide continues to grow driven by population growth and other factors such as obesity, low physical activity levels, dietary habits, smoking, and alcohol. Current estimates place the number of surgical procedures annually worldwide at greater than 230 million[6]; the majority in the areas of general, orthopaedic/trauma and obstetric/gynaecological surgery. The market for sedation and anaesthesia has been short on pharmaceutical development during the last decade and there remains room for innovation and development in standard of care. BYFAVO™ is fast acting and has a favourable safety profile based on the clinical studies in 966 patients who underwent procedural sedation for colonoscopies and bronchoscopies and similar procedures. It is estimated there are approximately 25 million GI procedures annually in the US.[7]

In addition, APD403 is currently in late-stage development for the management of nausea and vomiting in cancer patients receiving emetogenic chemotherapy. The cancer population continues to grow, due both to the increasing incidence of the condition in an ageing population and to the increasing longevity of cancer patients, as a result of earlier diagnosis and advances in cancer treatment. It is estimated that there were 18 million cancer cases worldwide in 2018 and this is expected to increase to 27 million in 2035.[8] The Directors believe there is an opportunity to provide hospital and clinic-based oncologists with a drug to better manage CINV which can enable optimal cancer treatment. APD403 is being specifically developed to meet what the Directors believe to be the key unmet need, late stage CINV, particularly late stage nausea.

2.2 *Near-market and late stage assets: two approved products, BARHEMSYS® and BYFAVO™, with imminent commercialisation opportunities and APD403 in late stage clinical development*

The FDA approved the NDA for BARHEMSYS® on 26 February 2020. The approved indications for BARHEMSYS® are: (i) treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or who have not received prophylaxis (at a dose of 10 mg); and (ii) prevention of PONV, either alone or in combination with an antiemetic of a different class (at a dose of 5 mg).

This label includes rescue treatment in patients who have failed prior prophylaxis, and combination prophylaxis with other antiemetics in higher risk patients, the two key commercial unmet needs. The Directors believe BARHEMSYS® will have a strong competitive position, as it is the first product specifically labelled for these uses.

The FDA approved the NDA for BYFAVO™ on 2 July 2020. The approved indication is the induction and maintenance of procedural sedation in adults. The safety and efficacy of BYFAVO™ has been evaluated in three Phase 3 trials in a total of 966 adult patients, with each study being randomised, double-blind, placebo and active controlled and multicentre.

Two Phase 2 clinical studies have been completed on APD403 for the management of CINV. The Company met with the FDA in April 2019 at which it was confirmed that one of the Phase 2 studies already completed would potentially be acceptable as a registrational trial and therefore that only one further, positive Phase 3 clinical trial may now be required to support registration in CINV, which is expected to be initiated in 2021.

2.3 *Poised to commercialise: key commercialisation rights and the opportunity to exploit the US market through the scale up of an efficient commercial infrastructure*

The Group holds all development and commercialisation rights to BARHEMSYS® and APD403 in all territories and the Directors believe they each have significant commercialisation potential. The Directors intend to focus on the direct commercialisation in the US of its own products and the in-licensed product, BYFAVO™.

The conditions being addressed by the Group's product candidates are primarily managed by the following medical specialists: anaesthesia and surgical procedure specialists in the case of BARHEMSYS® and BYFAVO™ and oncologists in the case of the APD403. It is estimated that in the US, 80 per cent of surgical procedures are performed in approximately 1,600 hospitals.[9] Based on current plans, the Company

---

[6] The Lancet: Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes.

[7] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). Please refer to Part II (*Risk Factors*) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

[8] Global Cancer Observatory, https://gco.iarc.fr/ (26/07/2020). International Journal of Cancer, 2018 Ferlay et al.

[9] Symphony Health, Source Non Retail, August 2017 – July 2018.

believes it can reach centres performing approximately 50 per cent of the surgical procedures with an initial sales force of approximately 30 field sales representatives at the initial launch of BARHEMSYS® and BYFAVO™. Each sales representative is expected to have its own sales territory covering accounts with greatest immediate opportunity. The Company expects to increase the sales force as demand for the product grows. The Group plans to leverage the sales and marketing infrastructure they will build to commercialise APD403 (for CINV) to oncologists, if approved.

2.4 *Strong intellectual property protection: BARHEMSYS® underpinned in the US by patent listing in the Orange Book and market exclusivity and BYFAVO™ protected by dosage regimen, polymorph and method of manufacture patents underpinned by Orange Book listing*

Amisulpride, the active ingredient within two of the Group's product candidates, had never been previously approved for use in the US. BARHEMSYS® therefore qualified to have the patents listed in the Orange Book which conveys for a minimum of five years' market exclusivity granted by the FDA upon approval of a new drug, with the potential for further extensions.

US patents have been granted describing the use of amisulpride for the management of PONV, CINV and opioid induced nausea and vomiting ("**OINV**"). Their initial terms run until 2031 and a patent term extension to February 2034 is currently being assessed by the US Patent and Trademark Office. The Company's granted PONV patents cover BARHEMSYS® and have been listed in the Orange Book, providing additional protection.

The patent families for BARHEMSYS® and APD403 have also been granted widely in other major pharmaceutical territories, including but not limited to, Europe, Japan and China. For further information on the Group's patent position see Section 9 of this Part VI (*Information on the Company and the Group*).

BYFAVO™ is protected by a number of issued and pending US patents. There are a number of other patents protecting the product, including polymorphic forms, manufacturing process and dosing regimen, some of which last to 2031. It is expected that a patent term extension request will be made in respect of one of these patents with a view to extending coverage to 2034. The patents should qualify to be listed in the Orange Book soon, now that approval has been obtained.

2.5 *Leadership to deliver the vision: strong management with demonstrable track record, supported by a syndicate of leading healthcare investors and Key Opinion Leaders (KOLs)*

The Group's management team has extensive experience in the discovery, development and commercialisation of hospital pharmaceutical products, in drug repurposing, business development and in corporate and financial control in public and private companies. In previous roles, members of the management team and Board successfully commercialised the branded post-operative pain product OFIRMEV®, which was launched into the US in a generic market, providing a similar value proposition to that proposed for BARHEMSYS® and BYFAVO™ to the same key customers (anaesthetists, surgical teams and directors of pharmacy). The team has successfully raised £43.0 million in private financing (which excludes any financing or proceeds realised from the BYFAVO™ Acquisition) and €38.1 million from the proceeds of the IPO (net of expenses) in March 2018 for the purposes of seeking BARHEMSYS® approval.

The Group has developed strong links with key opinion leaders, who have input into the Group's development programmes, providing a strong platform for validating clinical results and the opportunity for influential publications of the study results. The Company has worked with 14 of the 22 authors of the latest worldwide Consensus Guidelines on PONV[10] in connection with the development and commercialisation of BARHEMSYS®. Some of the KOLs with whom the Group already has strong relationships are also influential in the field of procedural sedation and have been involved in the development of BYFAVO™.

3. Strategy

The Group aims to become a leading hospital pharmaceutical organisation, providing products for hospital-based anaesthetists and surgical teams and hospital and clinic-based oncologists, initially through the development and US commercialisation of its current products. The key elements of this strategy are as follows:

[10] Gan et al., 2020.

3.1 *Directly commercialise BARHEMSYS® and BYFAVO™ in the US*

The Group received approval from the FDA to market BARHEMSYS® for the management of PONV, including the rescue treatment of PONV in patients who have received prior prophylaxis and combination prophylaxis in higher risk patients, the two key commercial unmet needs, on 26 February 2020. The FDA approval of BYFAVO™ for the management of procedural sedation was granted by the FDA on 2 July 2020.

The US is currently the largest market for pharmaceutical products and the Group is establishing its own sales and marketing infrastructure there, initially targeting hospital-based anaesthetists and surgical teams. The Group plans to focus initially on establishing BARHEMSYS® as a safe and effective rescue treatment for patients who suffer PONV despite prior prophylaxis with other antiemetics. The Directors believe that once surgical teams have experience of the efficacy and pharmacoeconomic benefits of BARHEMSYS® for rescue treatment, the product will be used earlier in the treatment pathway as part of a combination prophylaxis regimen for higher risk patients and those patients undergoing surgery where PONV could significantly adversely impact recovery or surgical outcomes. The Directors believe that BYFAVO™ can be promoted through the same sales channels as are targeted for BARHEMSYS® and the Group plans to launch both BARHEMSYS® and BYFAVO™ in the second half of 2020.

The Group's preliminary US commercialisation plans assume an employee base of up to 80, including the Group's existing 37 employees, an initial hospital sales force comprised of approximately 30 field sales representatives at commercial launch (anticipated in the second half of 2020) and a further 10 support staff. The Directors expect to increase the sales force to approximately 60 representatives within 3 years following launch depending on uptake of the products. Because a substantial portion of the prescribing activity arises in a relatively limited number of institutions, the Directors believe that the Group can successfully promote its products with such a sales force by focusing on those institutions that account for a substantial proportion of the hospital surgical market.

The adoption of hospital products typically requires the product firstly to be accepted on any institution's formulary of approved products before the product can be prescribed. This acceptance onto formulary typically requires the hospital's Pharmacy & Therapeutics Committee to be persuaded of the clinical and pharmacoeconomic benefits of the product.

The Directors will be monitoring near-term milestones to assess the launch progress for both products. Those milestones will include:

- the completion of the DEA scheduling of BYFAVO™;
- BARHEMSYS® product availability in the US supply chain and first commercial orders placed by wholesalers;
- the hiring of the field sales representatives;
- BYFAVO™ product availability in the US supply chain and first commercial orders placed by wholesalers;
- initial scheduling of the drugs for formulary review at hospitals in the US;
- subsequent approvals for the drugs to be placed on formulary at hospitals and surgical centers;
- initial stocking orders placed by hospitals; and
- accounts that have reordered the product.

The Directors believe these are key early indicators of future sales volumes and launch effectiveness.

3.2 *Establish commercialisation partnerships outside the US*

The Directors believe that markets outside the US are generally smaller and the processes for adoption of hospital products and establishing pricing and reimbursement can vary country by country. To focus its resources on the commercial opportunity in the US, the Group intends to enter into licensing and/or distribution agreements for BARHEMSYS® and APD403 outside the US where it is able to, and where commercially viable and regulatory approvals are obtained and for which any necessary consents are obtained, with selected pharmaceutical partners which already have the appropriate expertise and sales and marketing infrastructure. Initially the Group will focus on major pharmaceutical markets such as parts, or all, of Europe, with the aim of initiating discussions during 2020.

3.3 *Leverage the future commercial infrastructure through the addition of complementary products*

The Group intends to continue the development of APD403 for CINV. A US NDA submission could be made in late 2022 or early 2023 assuming development plans progress to the Group's expectations. With only a moderate increase in size of approximately 30 further employees, the initial sales infrastructure could also commercialise APD403.

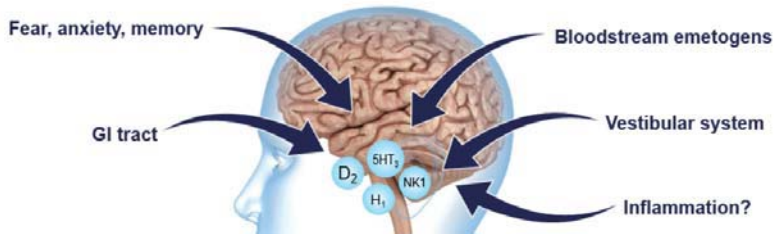
The Directors believe that once BARHEMSYS® and BYFAVO™ have been successfully established in the US market, the Group intends to assess additional, externally-sourced opportunities to exploit its US hospital sales and marketing infrastructure, including in-licensing or acquiring further complementary products or product candidates.

4. Product portfolio and commercial opportunities

Further information on BARHEMSYS®, BYFAVO™ and APD403 is presented in detail below, in each case describing the condition, market opportunity and unmet need, and development status and future plans.

4.1 *BARHEMSYS®*

(a) Nausea and vomiting



Nausea (feeling sick) is an unpleasant sensation of wanting to vomit. Vomiting (emesis or being sick) is the forceful expulsion of the contents of the stomach out through the mouth. Nausea and vomiting are mediated by collections of neurones in the brainstem, which receive signals from around the body, including from the gut; the vestibular apparatus in the ear, which controls balance; the cerebral cortex; and an area at the base of the brain called the *area postrema*, which can detect poisons in the bloodstream. Stimuli which can provoke nausea and vomiting are known as emetogenic, and can include toxins in the stomach or bloodstream (from bad food, chemicals or medicines, for example), excessive or disruptive movement, shocking or unpleasant sights or smells or even simply the thought or anticipation of such things. When emetogenic signals are received in the brainstem, further signals are sent via the nervous system to trigger the act of vomiting by the gut and/or the sensation of nausea.

The nerve pathways involved in nausea and vomiting involve several different neurotransmitters, including dopamine, serotonin (5-HT), acetylcholine, histamine and neurokinin-1 (also known as substance P). Drugs which can block the receptors used by these neurotransmitters, such as dopamine D_2-antagonists, serotonin $5\text{-}HT_3$ antagonists, antihistamines, NK1-antagonists, and so on, may be able to prevent or treat nausea and vomiting. Unfortunately, it is not possible to predict which one, or more, of these pathways will be involved in any patient and therefore which will have to be blocked to stop the nausea and vomiting response. As a consequence, the management of clinically important forms of nausea and vomiting, such as PONV and CINV, has evolved using combinations of antiemetic drugs from different mechanistic classes in an attempt to block as many of the pathways as possible. The management of PONV and CINV is described in more detail in Sections 4.1(c) and 4.4(b) of this Part VI (*Information on the Company and the Group*).

(b) Post-operative nausea and vomiting (PONV)

PONV is a common complication of surgery, occurring in approximately 30 per cent of surgical patients and up to 80 per cent of high-risk patients. Typically, two thirds of patients with PONV have nausea and one third have vomiting. The risk of PONV is higher for women, non-smokers, those who have experienced prior motion sickness or PONV, and those receiving post-operative opioid pain control. PONV is associated with the use of volatile anaesthetic gases and opioid analgesics and is particularly common following gynaecological, abdominal, breast, eye and ear operations, especially those lasting an hour or more. PONV most often starts in the first three hours after the end of anaesthesia, with a decreasing trend over 24 hours.[11]

[11] Gan et al., 2014, pages 85 to 113.

PONV is a significant issue for patients and healthcare providers. It has been ranked as the most undesirable of all surgical complications by patients and contributes significantly to patient anxiety and distress.[12] PONV can also delay hospital discharge, result in readmission after in-patient procedures and lead to day-case patients being admitted to hospital, all of which can result in significantly increased healthcare costs.[13] For example, in a study of 402 patients at Thomas Jefferson Hospital in Philadelphia, a reported 36 per cent of orthopaedic surgery patients experienced nausea or vomiting and had an associated 0.7 day increase (23 per cent) in their length of hospital stay.[14] With an estimated cost of a non-ICU hospital day of $2,658,[15] the additional economic cost of nausea and vomiting in these patients exceeds $1,800.[16]

(c) Current management of PONV

The latest PONV Consensus Guidelines[17] recommend that patients are assessed for their risk of suffering from PONV using a simple scoring system (one point for each of the four major risk factors for PONV (i) female, (ii) non-smoker, (iii) prior history of PONV or motion sickness and (iv) expected use of post-operative opioid pain control)[18] and are managed accordingly. It is recommended that patients at moderate risk of PONV (one or two risk factors) be given two prophylactic antiemetics to reduce the occurrence of PONV. In higher risk patients (three or four risk factors) it is recommended that 3 or 4 prophylactic antiemetics from different pharmacological mechanisms of action are given.

The mainstay of PONV prophylaxis (prevention) is the class of 5-HT_3 antagonists. Market research commissioned by the Group in the US indicates that ondansetron is the most frequently used 5-HT_3 antagonist, administered to approximately 69 per cent of those patients who receive any PONV prophylaxis.[19] In clinical trials, ondansetron has delivered a relative risk reduction compared to placebo in the range of 14 to 28 per cent.[20] In higher risk patients, a second antiemetic with a different mechanism of action is recommended to be added to the 5-HT_3 antagonist, the corticosteroid dexamethasone being the most common.[21] Dexamethasone, when added to ondansetron, has been shown to deliver a relative risk reduction of approximately 25 per cent compared to ondansetron alone.[22] This still leaves a significant number of patients whose PONV is not effectively managed, leaving an opportunity for an effective and safe antiemetic with a third mechanism of action that can be used prophylactically in combination with 5-HT_3 antagonists and dexamethasone in higher risk patients.[23] The use of antiemetics other than 5-HT_3 antagonists and corticosteroids (e.g. metoclopramide, promethazine and scopolamine) is limited due to safety concerns and/or limited efficacy data.[24] For example, droperidol, a dopamine antagonist, is an effective antiemetic and was formerly considered by experts to be the best available drug for preventing PONV.[25] However, since 2001, its use in the US has been greatly reduced[26] following the inclusion in its prescribing information of a boxed warning relating to cardiac toxicity, including serious and even fatal heart rhythm disturbances, arising from prolongation of the QT-interval.[27] In addition, it can cause extrapyramidal side effects ("**EPS**"), or movement disorders, and sedation.

Approximately a third of patients who are given PONV prophylaxis will still experience nausea and/or vomiting after their operation. In such cases, the PONV Consensus Guidelines recommend rescue treatment using an antiemetic with a different pharmacological mechanism of action to those that were previously given prophylactically.[28] Despite these recommendations, market research conducted by the Group indicates that, in about 70 per cent of cases, further ondansetron (a 5-HT_3 antagonist) is given as a rescue after it has already failed to achieve adequate prophylaxis, even though the ondansetron prescribing information clearly states that this is not an effective strategy. The Directors believe that this practice has been driven by the lack of safe and effective medications from other classes approved or suitable for PONV rescue, prior to the approval of BARHEMSYS®. For example, corticosteroids such as dexamethasone take a significant time to

[12] Koivuranta et al., 1997; Apfel et al., 1999, pages 693 to 700; Macario et al., 1999.
[13] Gan et al., 2014, pages 85 to 113.
[14] Pizzi et al., 2012, pages 502 to 514.
[15] Kaiser Family Foundation http://kff.org/other/state-indicator/expenses-per-inpatient-day/ (accessed 20 March 2020).
[16] Candrilli, 20 to 24 May, 2006.
[17] Gan et al., 2020.
[18] Apfel et al., 1999, pages 693 to 700.
[19] Acacia Pharma Market Research, November 2014, LSSG.
[20] Fortney et al., 1998; Apfel et al., 2004; Gan et al., 2011.
[21] Acacia Pharma Market Research, November 2014, LSSG.
[22] Apfel et al., 2004, pages 2441 to 2451.
[23] Acacia Pharma Market Research, November 2014, LSSG.
[24] Acacia Pharma Market Research, November 2014, LSSG.
[25] Gan et al., 2007, pages 1615 to 1628.
[26] Habib et al., 2008, pages 35 to 39.
[27] Droperidol Summary of Product Characteristics.
[28] Gan et al., 2020.

become effective as antiemetics and are therefore too slow-acting to be useful for rescue therapy; while the antihistamine promethazine causes sedation and can be challenging to administer intravenously, as it causes significant tissue damage in the event of extravasation; metoclopramide is a weak antiemetic, has a poor side effect profile, is not recommended in prescribing guidelines and has no rescue indication. The Directors therefore believe there is an opportunity for an effective and safe antiemetic with a third mechanism of action that can be used to rescue patients with established PONV who have failed prior prophylaxis with other antiemetics.

The popularity among physicians of the dopamine antagonist mechanism of action, coupled with significant safety concerns surrounding existing members of the class, led the Group to explore the possibility of developing an efficacious and safe dopamine antagonist to meet current needs. Clinical data have demonstrated that BARHEMSYS® avoids the safety concerns that limited the use of droperidol, whilst still being effective in reducing nausea and vomiting. Furthermore, BARHEMSYS® is the only antiemetic specifically approved for use as rescue therapy for patients with PONV who have failed standard prophylaxis, as well as for combination use with other antiemetics to prevent PONV. Therefore, BARHEMSYS® has the potential to be used: (i) to rescue patients with PONV who have not responded to standard antiemetic prophylaxis; and (ii) to prevent PONV in combination prophylaxis with standard antiemetics in higher risk patients.

(d) Competing product candidates in development

The Directors believe that there are no new agents in Late Stage clinical development for the management of PONV and that there are no other dopamine antagonists in any stage of clinical development for PONV.

(e) BARHEMSYS® product description

BARHEMSYS® (formerly referred to as APD421) comprises a low-dose (5 or 10 mg), intravenous injection formulation of amisulpride, a selective dopamine antagonist that has previously been approved in Europe, Australia, South America and other territories, but not the US, as an oral treatment for the management of schizophrenia and other psychoses, in a dose range of 50-1,200 mg per day. Prior to Acacia Pharma's submission of the BARHEMSYS® NDA, amisulpride had never been submitted for approval in the US for any therapeutic indication. BARHEMSYS® is differentiated from the existing marketed amisulpride products where they exist outside the US by its intravenous route of administration and dose.

Market research conducted with anaesthetists in the US and Europe indicated PONV was an unmet need.[29] The dopamine antagonist droperidol was anaesthetists' drug of choice for the management of PONV until it received a "boxed warning" for cardiac issues associated with QT prolongation in 2001.[30] As a consequence, the Group sought a dopamine antagonist that had been marketed without any cardiac safety concerns that could potentially be repurposed for the management of PONV. The Group also sought a dopamine antagonist with low potential for sedation and EPS. Amisulpride was selected primarily for its potency and its highly favourable safety profile, established during the previous two decades of widespread clinical use in psychiatry. In a review of 11 clinical trials involving 1,247 patients, of whom 905 were treated with an average daily dose of 670 mg for acute exacerbations of schizophrenia, no serious toxicity was reported. In particular, no cardiac disorder and only a low rate of EPS were reported, which was not significantly different from placebo treatment.[31] The low potential of amisulpride to cause cardiac toxicity was further confirmed by the Group in an electrophysiological study which showed that the blockade by amisulpride of the cardiac hERG channel, an important determinant of rhythm disturbances, was 440 times weaker than by droperidol.

Having determined that amisulpride appeared to have the appropriate safety profile, the Group conducted pre-clinical efficacy studies confirming the drug's antiemetic potential and has confirmed it in subsequent clinical studies. Of particular note, the label for BARHEMSYS® approved by the FDA does not include a boxed warning, unlike the labels for other dopamine antagonists sometimes used in PONV management, such as droperidol, haloperidol and metoclopramide.

The Group filed patent applications describing the new use of amisulpride for the management of PONV in major pharmaceutical territories. These applications have subsequently been granted in key pharmaceutical territories, such as the US and Europe. Additional selection patent applications have now been filed based on data generated in Phase 3 clinical trials. Further information on the status of the Group's patents and patent applications can be found in Section 9 of this Part VI (*Information on the Company and the Group*).

---

[29] Acacia Pharma Market Research, Bridgehead International, 2008.
[30] Gan et al., 2007, page 1620.
[31] Coulouvrat et al., 1999, pages 209 to 218.

(f) BARHEMSYS® development

The primary clinical development of BARHEMSYS® was completed in 2018, with the safety and efficacy of BARHEMSYS® in the management of PONV having been evaluated in 3,388 patients and healthy volunteers, of whom 1,999 received BARHEMSYS®. Data from the clinical programme were used to support the submission of an NDA and subsequent approval by the FDA for the indications:

(i) treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or who have not received prophylaxis (at a dose of 10 mg); and

(ii) prevention of PONV, either alone or in combination with an antiemetic of a different class (at a dose of 5 mg).

The nine clinical studies included in the submission are described below.

Pivotal Clinical Studies

DP10019. Phase 3 treatment study in patients who have received prior antiemetic prophylaxis, conducted in the US, Canada and Europe.

This study, now published in the literature,[32] was a double-blind randomised comparison of 5 mg and 10 mg BARHEMSYS® and placebo as treatment for established episodes of PONV in patients who had received prior PONV prophylaxis and was conducted at 23 centres in the US, Canada, Germany and France. A total of 702 adult patients who developed PONV after surgery involving a general anaesthetic, despite having received prior antiemetic prophylaxis, were randomised on a 1:1:1 basis to receive a single intravenous injection of 5 mg or 10 mg BARHEMSYS® or a matching placebo (defined as the mITT population). The primary endpoint was the successful treatment of the episode of PONV, with Complete Response (CR) defined as no recurrence of vomiting (excluding the first 30 minutes after treatment) and no requirement for further antiemetic rescue medication, in the 24-hour period after treatment. In the mITT population, BARHEMSYS® 10 mg was superior to placebo in terms of CR (41.7 per cent vs 28.5 per cent, p=0.003 after adjustment for multiplicity). The 5 mg dose of BARHEMSYS® was somewhat superior to placebo but the benefit generally did not reach statistical significance.

mITT population	**Placebo**		**5 mg BARHEMSYS®**		**10 mg BARHEMSYS®**	
Number of subjects	235		237		230	
Primary Endpoint Complete Response†	**67**	**28.5%**	**80**	**33.8%**	**96**	**41.7%****
Secondary Endpoints						
Vomiting	67	28.5%	43	18.1%**	36	15.7%***
Rescue medication use	163	69.4%	155	65.4%	127	55.2%***
Nausea burden‡ 0-180 mins	7629		6995		5638***	

p≤0.01*p≤0.001 (one-sided p values)

† No emesis in 30 min-24 hours after treatment or use of rescue medication in 0-24 hours after treatment.

‡ Area under the curve of nausea scores

The proportion of patients reporting one or more treatment-emergent adverse events was lower in both the 5 mg and 10 mg BARHEMSYS® groups (42.2% and 43.0% respectively) than the placebo group (48.1%). There was no material difference between the groups in the incidence of serious, severe or life-threatening adverse events. Patients in the BARHEMSYS® group whose PONV occurred in the post-anaesthesia care unit (PACU), an especially high-cost area of the hospital, spent on average 141 minutes in the PACU compared to 176 minutes for those in the placebo group, a reduction of 35 minutes. The overall duration of hospital stay was on average 50 hours for the BARHEMSYS® group compared to 56 hours for the placebo group.

This study confirms that a 10 mg dose of intravenous BARHEMSYS® can safely and effectively treat established episodes of PONV in surgical patients who have had prior PONV prophylaxis, leading to reduced hospital occupancy, and the Directors therefore believe that BARHEMSYS® will be an attractive clinical choice and commercial opportunity in that patient population. The Directors believe this is the first ever randomised trial that has shown successful rescue of PONV in patents that have previously failed antiemetic prophylaxis.

[32] Habib, A.S. et al., 2019.

DP10018. Phase 3 treatment study in the absence of prior antiemetic prophylaxis conducted in the US and Europe.

This study, now published in the literature,[33] was a double-blind randomised comparison of 5 mg and 10 mg BARHEMSYS® and placebo as treatment for established episodes of PONV in patients who had not received prior PONV prophylaxis and was conducted at 21 centres in the US, Canada, Germany and France. A total of 560 adult surgical patients who developed PONV after surgery involving a general anaesthetic, having received no prior PONV prophylaxis, were randomised on a 1:1:1 basis to receive a single intravenous injection of 5 mg or 10 mg BARHEMSYS® or a matching placebo (defined as the mITT population). The primary endpoint was the Complete Response (CR), defined as successful treatment of the episode of PONV, with no recurrence of vomiting (excluding the first 30 minutes after treatment) and no requirement for further antiemetic rescue medication, in the 24 hour period after treatment. In the mITT population, BARHEMSYS® 5 mg and BARHEMSYS® 10 mg both achieved CR in 31.4 per cent of patients, compared to 21.5 per cent for placebo (p=0.016 after adjustment for multiplicity). Rescue medication use was significantly lower in both BARHEMSYS® groups than placebo, as was the amount of nausea experienced by patients in the first 180 minutes after treatment.

mITT population	**Placebo**		**5 mg BARHEMSYS®**		**10 mg BARHEMSYS®**	
Number of subjects	181		191		188	
Primary Endpoint Complete Response†	**39**	**21.5%**	**60**	**31.4%***	**59**	**31.4%***
Secondary Endpoints						
Vomiting	62	34.3%	64	33.5%	57	30.3%
Rescue medication use	135	74.6%	121	63.4%**	119	63.3%**
Nausea burden‡ 0-180 mins	7559		6470*		6512*	

*p≤0.025**p≤0.01 (one-sided p values)

† No emesis in 30 min-24 hours after treatment or use of rescue medication in 0-24 hours after treatment.

‡ Area under the curve of nausea scores

The proportion of patients reporting one or more treatment-emergent adverse events was lower in both the 5 mg and 10 mg BARHEMSYS® groups (39.8% and 42.0% respectively) than the placebo group (53.0%). There was no material difference between the groups in the incidence of serious, severe or life-threatening adverse events.

This study confirms that both a 5 mg and 10 mg dose of intravenous BARHEMSYS® can safely and effectively treat established episodes of PONV in surgical patients who have not had prior PONV prophylaxis.

DP10017. Phase 3 combination prophylaxis study conducted in the US and Europe.

This study, now published in the literature,[34] was a double-blind randomised comparison of BARHEMSYS® at 5 mg and matching placebo, in combination with another non-dopaminergic antiemetic (such as ondansetron or dexamethasone), as prophylaxis of PONV in higher risk, adult, surgical patients, conducted at 29 centres in the US, Germany and France. A total of 1,147 adult surgical patients with three or four PONV risk factors, undergoing in-patient or out-patient surgery under general anaesthesia lasting at least one hour, were randomised on a 1:1 basis to receive a single intravenous injection of either 5 mg BARHEMSYS® or a matching placebo in combination with another antiemetic (defined as the mITT population). The primary efficacy endpoint was Complete Response (CR), defined as no episodes of vomiting or retching or requirement for antiemetic rescue medication in the 24 hours after the end of surgery. Nausea was regularly assessed and any spontaneously reported nausea recorded. The groups were well balanced for baseline characteristics, including overall risk profile. In the mITT population, BARHEMSYS® was significantly superior to placebo in terms of CR (57.7 per cent vs. 46.6 per cent, p‹0.001), representing a 21 per cent relative risk reduction (RRR). Individual rates of emesis, nausea and rescue medication use were all significantly lower in the BARHEMSYS® group than the placebo group. The time to failure (emergence of PONV) was statistically significantly longer in the BARHEMSYS® group compared with the placebo group (p‹0.001).

[33] Candiotti KA, Kranke P, Bergese SD, et al., 2019.

[34] Kranke et al., 2018.

mITT population	Placebo + other antiemetic		5 mg BARHEMSYS® + other antiemetic	
Number of subjects	575		572	
Primary Endpoint Complete Response†	**268**	**46.6%**	**330**	**57.7%*** **
Secondary endpoints				
Vomiting	115	20.0%	79	13.8%**
Rescue medication use	284	49.4%	234	40.9%**
Significant nausea	274	47.7%	212	37.1%***
Any nausea	335	58.3%	286	50.0%**

p≤0.01*p≤0.001 (two-sided p values)

† No emesis or use of rescue medication in 0-24 hours after surgery.

Somewhat fewer patients in the BARHEMSYS® group experienced one or more treatment-emergent adverse events (44.9%) than in the placebo group (52.7%). There was no material difference between the groups in the incidence of serious, severe or life-threatening adverse events.

This study confirms that a 5 mg dose of intravenous BARHEMSYS® added to commonly used anti-emetics is more effective than commonly used anti-emetics on their own, with no safety concerns arising from the combination use. The Directors therefore believe that BARHEMSYS® would be an attractive clinical choice as part of a combination antiemetic regimen for preventing PONV in surgical patients at moderate to high risk of suffering PONV.

DP10015. Phase 3 monotherapy prophylaxis study conducted in the US.

This study, now published in the literature[35] in conjunction with study DP10014, was a randomised, double-blind, placebo-controlled Phase 3 study, comparing 5 mg BARHEMSYS® to placebo as prevention of PONV, conducted at nine centres in the US, of which eight contributed evaluable patients. A total of 342 adult surgical patients undergoing procedures expected to last at least one hour under standard inhalational anaesthesia, with two or more risk factors for PONV, were randomised on a 1:1 basis to receive a single intravenous injection of 5 mg BARHEMSYS® or a matching placebo, given over 1-2 minutes at the time of induction of anaesthesia. The primary efficacy endpoint was complete response, defined as no episodes of vomiting or retching or requirement for antiemetic rescue medication in the 24 hours after the end of surgery. Nausea was regularly assessed and any spontaneously reported nausea recorded. The groups were well balanced for baseline characteristics, including overall risk profile. In the modified intent to treat (mITT) analysis of all 342 dosed patients, BARHEMSYS® was significantly superior to placebo in terms of complete response (44.3 per cent vs. 32.5 per cent, p=0.013), with BARHEMSYS® showing a 17.5 per cent relative risk reduction. Secondary endpoints, including incidence of rescue medication use, time to PONV and time to first use of rescue medication, were significantly improved by BARHEMSYS®. The incidence of rescue medication use was reduced from 66.9 per cent to 54.5 per cent (p=0.010), as shown in the table below, while median time to onset of PONV (failure of prophylaxis) increased from 341 minutes with placebo to 752 minutes with BARHEMSYS® (p=0.004) and median time to first rescue medication use increased from 371 to 859 minutes (p=0.003).

[35] Gan et al., 2017.

mITT population	Placebo		5 mg BARHEMSYS®	
Number of subjects	166		176	
Primary Endpoint Complete Response†	**54**	**32.5%**	**78**	**44.3%***
Secondary Endpoints				
Vomiting	37	22.3%	35	19.5%
Rescue medication use	111	66.9%	96	54.5%**
Significant nausea	82	49.4%	69	39.2%*
Any nausea	102	61.4%	94	53.4%

*p≤0.05**p≤0.01 (two-sided p values)
† No emesis or use of rescue medication in 0-24 hours after surgery.

There was no significant difference in the overall rate of adverse events between BARHEMSYS® and placebo treated subjects and no notable side effects were reported with BARHEMSYS®. In particular, no extrapyramidal toxicity or significant other central nervous system or cardiovascular toxicity were reported. The only difference in any safety parameter was that serum prolactin was increased post-operatively to a greater extent in the BARHEMSYS® group than in the placebo group, a well-known effect of dopamine-antagonists. The average rise was small, the mean post-treatment value in the BARHEMSYS® group still being within the normal range for non-pregnant females, and was not associated with any clinical consequences.

Supporting Clinical Studies

DP10006. Phase 2 dose ranging, monotherapy prophylaxis study.

This study, now published in the literature,[36] was a randomised, double-blind, placebo-controlled, dose-ranging Phase 2 study, conducted in ten sites in France, Germany and the US. A total of 215 subjects at moderate to higher risk of PONV (defined as having at least two of the four major risk factors for PONV) and undergoing elective, in-patient surgical operations lasting at least an hour under general anaesthesia, were randomised to receive one of three doses (1 mg, 5 mg and 20 mg) of BARHEMSYS® or a matching placebo, given as a single intravenous injection at the induction of anaesthesia (defined as the mITT population). The primary endpoint was complete response (defined as no episodes of vomiting or retching and no requirement for antiemetic rescue medication) during the 24 hours after the end of surgery. Complete response was less frequent in the placebo group (17/54, 31.5 per cent) than in all the BARHEMSYS® groups (1 mg: 30/58, 51.7 per cent; 5 mg: 30/50, 60.0 per cent; 20 mg: 23/53, 43.4 per cent). The benefit reached statistical significance for the 1 mg (p=0.048) and 5 mg (p=0.006) groups, but not the 20 mg group. The 5 mg dose gave a relative risk reduction of 42 per cent compared to placebo. A statistically significant benefit was also seen for the 5 mg BARHEMSYS® dose in terms of vomiting (reduced from 35.2 to 14.0 per cent, p=0.006), nausea (reduced from 74.1 to 46.0 per cent, p=0.002), significant nausea (reduced from 48.1 to 24.0 per cent, p=0.005) and use of rescue medication (reduced from 66.7 to 38.0 per cent, p=0.002). BARHEMSYS® was very well tolerated by subjects at all three dose levels, with no significant difference in the rate of adverse events for any dose of BARHEMSYS® compared to placebo treated subjects. In particular, no extrapyramidal toxicity or significant other central nervous system or cardiovascular toxicity was reported. There was evidence of a "U-shaped" dose response curve similar to that observed in pre-clinical studies.

DP10014. Phase 3 monotherapy prophylaxis study conducted in Europe.

This study was a randomised, double-blind Phase 3 study of essentially identical design to study DP10015, and has been published in the literature[37] in conjunction with that study. It was conducted at six centres in Germany and four in France and involved 347 adult, surgical patients randomised on a 1:1 basis to receive either 5 mg BARHEMSYS® or placebo (defined as the mITT population). The efficacy endpoint considered most relevant by the FDA was complete response, defined as no episodes of vomiting or retching and no requirement for antiemetic rescue medication during the 24 hours after the end of surgery. In the mITT population, complete response occurred more frequently in the 5 mg BARHEMSYS® group than in the

[36] Kranke et al., 2013.
[37] Gan et al., 2017.

placebo group (59.2 per cent vs. 50.0 per cent, p=0.043). The incidence of nausea was significantly lower in the BARHEMSYS® group than the placebo group (44.4 per cent vs. 55.1 per cent; p=0.023). The incidences of emesis, significant nausea and rescue anti-emetic use were all lower in the BARHEMSYS® group than in the placebo group, but the difference in each case did not reach statistical significance. There were no significant differences in the safety profile of BARHEMSYS® and placebo.

DP10013. Thorough QT study.

This study, now published in the literature,[38] was a randomised, double-blind, four-period, crossover, "thorough QT" study to investigate the effect of intravenous BARHEMSYS® on cardiac conduction compared to placebo, in which 40 healthy adult subjects received 5 mg BARHEMSYS®, infused over two minutes, and 40 mg BARHEMSYS®, infused over eight minutes. It was conducted in a specialist Phase 1 unit in the UK. For each subject, the QT interval was placebo-corrected and compared to baseline at multiple time points between two minutes and 24 hours after the start of the BARHEMSYS® infusion. Following the 5 mg dose, the highest average change in QTc compared to baseline was 5.0 ms (upper bound of two-sided 90 per cent or one-sided 95 per cent confidence interval: 7.1 ms), occurring at eight minutes after the start of infusion. This is well below the regulatory threshold of concern, specified in ICH guidance document E14 in the following terms: "A negative 'thorough QT/QTc study' is one in which the upper bound of the 95 per cent one-sided confidence interval for the largest time-matched mean effect of the drug on the QTc interval excludes 10 ms. This definition is chosen to provide reasonable assurance that the mean effect of the study drug on the QT/QTc interval is not greater than around 5 ms". By 30 minutes, the average change was down to 2.1 ms. This is considered to indicate a very low clinical risk of torsade de pointes. After the supratherapeutic 40 mg dose, the highest average change in QTc was 23.4 ms. This QTc profile is similar to that of ondansetron, the most widely used antiemetic for PONV management, which showed a highest average QTc prolongation of 19.5 ms at a dose eight times greater than the standard PONV dose. Based on these data, the FDA-approved label for BARHEMSYS® includes warning language relating to QT effect similar to that in the label of ondansetron, the most widely used antiemetic, and, crucially, does not include a boxed warning, unlike droperidol.

DP10022. Phase 1 clinical pharmacology study on PK and QT effects of 10 mg BARHEMSYS®, alone and in combination with ondansetron.

This clinical pharmacology study, was conducted in 30 healthy volunteer in a specialist Phase 1 trials unit in the UK in Q3 2018. The average maximum effect on the QTc interval of a single 10 mg dose of BARHEMSYS®, infused over one minute, was 5.2 milliseconds (90% confidence interval 3.53-6.96 milliseconds). When a standard 4 mg dose of IV ondansetron was given at the same time, the average maximum effect was 7.3 milliseconds (90% confidence interval 5.48-9.16 milliseconds). The internationally agreed threshold level of regulatory concern for serious arrhythmias, such as torsade de pointes, is a mean effect on QTc of 10 milliseconds. The study also demonstrated that a second 10 mg dose of BARHEMSYS®, given two hours after the first, had a similar pharmacokinetic profile and did not significantly affect the QT or clinical safety profile of the drug. No serious adverse events were reported in the trial and there was no material difference in safety profile between BARHEMSYS® (with or without concomitant ondansetron) and placebo.

DP10020. Phase 1 metabolism and elimination study.

This clinical pharmacology study investigated the metabolism and elimination of radio-labelled BARHEMSYS®, given intravenously to six healthy volunteers. The study was conducted at a specialist Phase 1 unit in the Netherlands. The mean recovery of radioactivity in excreta was 96.4% (range 92.0-98.5%), of which 73.6% (range 70.6-79.2%) was recovered from urine and 22.8% (range 18.9- 25.7%) from faeces. BARHEMSYS® was predominantly excreted unchanged in urine and faeces, accounting for 57.5% of the dose excreted in urine in the first 48 hours and 20.6% of the dose excreted in faeces in the first 96 hours. Four metabolites were detected, formed by oxygenation, N-dealkylation, oxygenation plus di-dehydrogenation or methylation plus dehydrogenation and oxygenation plus dehydrogenation. The metabolites together represented 15.0% of the dose excreted in urine in the first 48 hours and 6.1% of the dose excreted in faeces in the first 96 hours. Excretion was initially rapid, with about two-thirds of the drug eliminated within 12 hours, primarily in urine. Urinary excretion was 94% complete after 24 hours. Thereafter, excretion was slower and predominantly in the faeces, with 76% of faecal excretion occurring in the period 24-72 hours. Excretion was essentially complete by 96 hours after dosing. These data are consistent with data on intravenous amisulpride previously published in the literature.[39]

[38] Taubel et al., 2017.
[39] Canal et al., 2002.

Clinical Pharmacokinetics of BARHEMSYS®

Comprehensive data on the clinical pharmacokinetics of BARHEMSYS® have been generated in the above study programme and in standard pre-clinical experiments.

BARHEMSYS® has a half-life of 4-5 hours, ensuring that adequate blood levels are present for 24 hours after administration. The peak plasma concentration of amisulpride delivered by a single 5 mg and 10 mg dose is 200 ng/mL and 357 ng/mL, respectively. This is less than that delivered by a single 200 mg oral tablet of amisulpride (424 ng/mL),[40] a dose currently approved in many countries worldwide. The total exposure delivered by BARHEMSYS®, measured by the area under the concentration-time curve, is 154 ng.h/mL for a 5 mg dose and 228 ng.h/mL for a 10 mg dose, an order of magnitude lower than the 3,549 ng.h/mL delivered by a single 200 mg oral dose of amisulpride.

BARHEMSYS® exhibits low plasma protein binding and neither inhibits nor induces the cytochrome P450 enzyme system. This makes the probability of drug-drug interactions involving BARHEMSYS® low.

(g) Regulatory path to approval

The Group originally submitted an NDA seeking approval from the US FDA to market BARHEMSYS® for the management of PONV in October 2017. The NDA was approved by the FDA on 26 February 2020.

The label for BARHEMSYS® is a broad differentiated label which includes the following therapeutic indications:

– BARHEMSYS® single 10 mg dose: treatment of established PONV in patients who have received antiemetic prophylaxis with an agent of a different class or no prior prophylaxis;

– BARHEMSYS® single 5 mg dose: prevention of post-operative nausea and vomiting (PONV), either alone or in combination with other antiemetics.

The Directors believe this to be the optimal initial label for securing rapid adoption of BARHEMSYS® onto hospital formularies in the US, based on research with a sample of hospital pharmacy directors and P&T committee members. The Directors are not aware of any other antiemetic with such a broad label in PONV and specifically with a label for rescue therapy in patients with PONV who have failed standard prophylaxis.

BARHEMSYS® comprises amisulpride formulated in pH-adjusted aqueous buffer, filtered into stoppered glass vials and terminally sterilised. More than 20 batches of BARHEMSYS® have been manufactured at a range of strengths and scales, including at the full commercial scale, demonstrating the robustness of the manufacturing process. Based on the strong stability data generated, a shelf-life of five years at room temperature has been granted. The first commercial lots of BARHEMSYS® have been manufactured, labelled and packaged and were shipped to the US during July 2020. Further batches are required to be manufactured in order to fully commercialise BARHEMSYS® although the future manufacturing costs are estimated by the Directors to be less than 10 per cent of the proposed sales price. A paediatric study plan has been agreed with the FDA in accordance with US regulations and is expected to be initiated in 2021.

(h) BARHEMSYS® commercial opportunity

The Directors estimate that approximately 65 million antiemetic eligible surgical procedures that require injectable analgesia, primarily opioids, are conducted each year in the US.[41] The Directors believe that use of injectable analgesia is a good surrogate for those procedures that could require antiemetics. Use of injectable analgesia is indicative of a relatively invasive procedure and the use of opioids, the most common type of analgesia, is in itself a risk factor for PONV.[42] Based upon market research commissioned by the Group, the Directors estimate that approximately 49 million patients receiving preventative antiemetics and approximately 16 million rescue events occur each year in the US, resulting in a total available market of approximately 65 million antiemetic treatment events per year.[43]

---

[40] MHRA: UK Pharmaceutical Assessment Report for amisulpride tablets, 2010.

[41] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005. Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

[42] Gan et al., 2020.

[43] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows: National Hospital Discharge Survey, 2006; National Survey of Ambulatory Surgery, 2006 (as revised in 2009); Source Healthcare; NCHS 2005. Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*.

Global consensus treatment guidelines recommend combination antiemetic prophylaxis for patients that have one or more risk factors for PONV.[44] According to market research commissioned by the Group in 2014 in the US, 40 per cent of surgical patients are considered at moderate risk of PONV (26 million) and 28 per cent are at high risk (18 million), and therefore eligible for combination antiemetic prophylaxis.[45] Data collected by the Society for Ambulatory Anesthesia (SAMBA) Clinical Outcomes Registry in the US provide similar estimates for the distribution of moderate-risk (45 per cent) and high-risk (25 per cent) patients.[46]

Physicians also reported in market research that up to 31 per cent of surgical patients who receive antiemetic prophylaxis suffer breakthrough episodes of PONV and receive rescue treatment, most commonly ondansetron.[47] In a pivotal study of 4,123 patients published in the New England Journal of Medicine, 40% of patients across risk and treatment strata required rescue antiemetic therapy.[48] Based upon these studies and clinical trials conducted with BARHEMSYS®, the Directors estimate that 32 per cent of patients (approximately 16 million patients) require rescue treatment for PONV each year. Current literature indicates that patients requiring rescue antiemetic therapy receive an average of two rescue doses per treatment event (approximately 32 million doses).[49]

The Group intends to market BARHEMSYS® for targeted patient populations, initially in patients requiring rescue treatment of PONV despite having received prior prophylaxis, and subsequently for higher risk patients requiring combination prophylaxis. Therefore, the Directors estimate the total target available market for rescue treatment and combination prophylaxis comprises an estimated 34 million treatment events (comprised of 16 million rescue events and 18 million prophylaxis events) and an estimated 50 million doses (comprised of 32 million rescue doses and 18 million prophylaxis doses) each year in the US.

The current US PONV market consists primarily of generic drugs, principally ondansetron and dexamethasone. US hospitals are typically not reimbursed separately for pharmaceuticals administered to the in-patient population (approximately 42 per cent of targeted surgical procedures), but rather are reimbursed a fixed fee for each surgical procedure conducted within a diagnosis related group (DRG). However, injectable medications administered in an out-patient setting (approximately 58 per cent of targeted procedures) could be eligible for separate reimbursement. While the Group anticipates that BARHEMSYS® will be utilised in both in-patient and out-patient settings and therefore subject to the respective reimbursement environments for each, the reimbursement strategy has been to assume that there would be no separate reimbursement for the drug and that both in-patient and out-patient surgical centres would utilise the drug and manage the costs out of the bundled payment received for the procedure due to the pharmacoeconomic and clinical benefits associated with its utilisation.

In the market research conducted by the Group in the last quarter of 2014, using a target product profile similar to BARHEMSYS®, physicians indicated an intention to adopt such a product in their practice for rescue treatment and prophylaxis treatment of moderate and high-risk patients. Physicians indicated that they would expect a maximum utilisation rate of such a product of 61 per cent for rescue treatment and prophylaxis of their higher risk patients, based on a target product profile anticipating a relative risk reduction of 22 per cent and 23 per cent respectively.[50]

In the second half of 2014, the Group commissioned a study of hospital pharmacy directors and physician members of hospital formulary committees to determine the pricing and market access opportunity for BARHEMSYS® for the rescue treatment and prevention of PONV in the US.[51] Respondents indicated that at a price of $80 they expected to place a drug with a target product profile similar to BARHEMSYS® on formulary for rescue treatment in over 80 per cent of hospital beds. Respondents were willing to pay $60 for combination prophylaxis treatment of high risk patients.[52] This preliminary determination has been supported by a qualitative pricing study conducted by the Group in the second half of 2018 and a further quantitative pricing study completed in Q1 2019. The Company currently anticipates, therefore, pricing a 10 mg dose of BARHEMSYS® for rescue treatment at approximately $80, and a 5 mg dose for combination prophylaxis at approximately $40. The Company continues to monitor the market and the final pricing will be announced at the product launch.

---

[44] Gan et al., 2020.
[45] Acacia Pharma Market Research, November 2014, LSSG.
[46] Glass et al., 2013.
[47] Acacia Pharma Market Research, November 2014, LSSG.
[48] Apfel et al., 2004.
[49] Chang et al., 2005.
[50] Acacia Pharma Market Research, November 2014, LSSG.
[51] Acacia Pharma Market Research, November 2014, ICON.
[52] Acacia Pharma Market Research, November 2014, ICON.

Data generated in DP10019, the Phase 3 rescue treatment study, indicated that patients receiving BARHEMSYS® were able to move out of the highly expensive post-anaesthesia care unit (PACU) into general hospital rooms 35 minutes more quickly, and one in four patients left hospital a day earlier. Given that each minute in the PACU is estimated to cost $9.52[53] and the average cost of an in-patient hospital stay is $2,658 per day in the US[54], this would equate to an estimated savings of $780 for each rescue patient dosed with BARHEMSYS® if priced at $80, a nine times return to the hospital. BARHEMSYS® also fits in auto-dispensing (Pysix™) machines, providing for ease of distribution.

4.2 BYFAVO™

(a) Procedural Sedation & Anaesthesia Market

Procedural sedation is a technique of administering sedatives or dissociative agents, with or without analgesics, to induce a state that allows the patient to tolerate unpleasant procedures such as colonoscopy while maintaining cardiorespiratory function.

General anaesthesia leads to loss of consciousness and loss of sensation of patients through the administration of anaesthetics in combination with opioid analgesics. This enables medical procedures such as major surgery, that would otherwise be unbearable, to be carried out with minimal discomfort or added risk.

The number of surgical procedures worldwide continues to grow driven by population growth and other factors such as obesity, low physical activity levels, dietary habits, smoking, and alcohol. Current estimates place the number of surgical procedures annually worldwide at greater than 230 million[55]; the majority in the areas of general, orthopaedic/trauma and obstetric/gynaecological surgery.

The market for sedation and anaesthesia has been short on pharmaceutical development during the last decade and there remains room for innovation. Sedative and anaesthetic safety is continuously reviewed as part of quality assessments and includes such elements as efficacy, unintended intra-operational awareness, respiratory depression, hemodynamic stability, post-operative/procedure emergence and recovery, long term effects of anaesthesia and patient morbidity.

The NDA for BYFAVO™ was based on use in procedural sedation for colonoscopies and bronchoscopies. It is estimated there are approximately 25 million GI procedures annually in the US[56] with over 80% administered by anaesthesia providers.[57] The broad label granted for BYFAVO™, covering all adult patient procedures lasting less than 30 minutes, makes it applicable for use in a range of other settings such as interventional radiology (over 6 million procedures per year)[58], ophthalmic (approximately 4 million procedures per year)[59] and plastic surgery procedures (approximately 1.5 million per year)[60], bringing the total number of procedures for which BYFAVO™ is suitable to approximately 40 million.

(b) Current Management of Procedural Sedation and Competition

Midazolam (Versed): Midazolam, a benzodiazepine, is an anaesthetic adjunct which is one of the most popular drugs used for sedation, usually given with an opioid, and is considered the standard of care against which other drugs are compared. Its popularity is in part due to its perceived haemodynamic safety and easy administration and titration. Disadvantages include its risk of respiratory depression and its relatively slow onset and offset of action, with unpredictability of effect caused by a slowly eliminated, active metabolite), leading to slower recovery of neuropsychiatric functions. Possible advantages of BYFAVO™ over midazolam include speed of onset and offset, leading to shorter times to initiation of procedures and post-procedure recovery and discharge, as well as fewer cardiorespiratory and other adverse events.

---

[53] Habib A, Curr Med Res Opin 2006; 22(6): 1093-1099 (cost adjusted for inflation to Jan 2020 using CPI data for Inpatient Hospital Services).
[54] Kaiser Family Foundation http://kff.org/other/state-indicator/expenses-per-inpatient-day/ (accessed 20 March 2020).
[55] The Lancet: Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes.
[56] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*.).
[57]Calculations based on available procedural data, applied Compound Annual Growth Rate from: Report on interventional Radiology November/December 2007.
[58]Calculations based on available procedural data, applied Compound Annual Growth Rate from: Report on interventional Radiology November/December 2007.
[59]Calculations based on available procedural data, applied Compound Annual Growth Rate from: American Medical Association 2011.
[60]Calculations based on available procedural data, applied Compound Annual Growth Rate from: American Society of Plastic Surgeons 2018.

Propofol (Diprivan): Propofol is a local anaesthetic used for procedural sedation. It has a rapid onset and offset of action and can be titrated very precisely. Its short half-life and limited "hang-over" effect have made it a popular choice amongst healthcare providers. It does have a narrow therapeutic window, though, and can cause severe and even fatal adverse reactions, including hypotension and respiratory depression. It can also cause pain on injection. Because there is no reversal agent, propofol generally requires very close and careful monitoring of patients throughout its use. Advantages of BYFAVO^{TM} over Propofol may include superior haemodynamic impact and effect on respiration and the availability of a reversal agent.

Dexmedetomidine (Precedex): Dexmedetomidine is used as an alternative to benzodiazepine sedatives in some cases. It is an alpha-2 antagonist which brings about sedative, analgesic, and anxiolytic properties. Potential advantages include increased patient and provider satisfaction, better cooperation of the patient, and no anxiety and agitation. Lack of respiratory compromise has been recognized as an advantage as well as ease of administration. Limitations include profound and complex effects on blood pressure and a long duration of action that may lead to slower recovery.

New compounds in development

Since the introduction of propofol in 1986, a number of new compounds have been evaluated for procedural sedation with a view to avoiding certain of the side-effects seen with propofol, particularly respiratory depression. However, to the best of the Directors' knowledge, only one new agent, Alfaxalone, is currently in development. Alfaxalone, a steroid which was first introduced in 1972 and withdrawn in 1984 because of hypersensitivity to the Cremophor EL solvent used, has been reformulated in a new cyclodextrin solvent by the Australian company Drawbridge Pharmaceuticals. It has completed the 15-patient pilot portion of a Phase 3 trial in maintenance of general anesthesia. No specific procedural sedation trials have yet been conducted.

(c) BYFAVO^{TM} product description

Remimazolam is an ultra-short-acting intravenous benzodiazepine sedative now approved by the FDA for procedural sedation in adults undergoing procedures lasting less than 30 minutes. In the human body, remimazolam is rapidly metabolized to an inactive metabolite by tissue esterases rather than by hepatic cytochrome-P450 pathways. Like other benzodiazepines, remimazolam can be reversed with flumazenil to rapidly terminate sedation if necessary. During clinical studies, remimazolam demonstrated efficacy and safety with approximately 2,400 volunteers and patients. Remimazolam has a rapid onset and offset of action combined with a favourable cardio-respiratory safety profile.

In January 2020, remimazolam was approved in Japan, where it is licensed to Mundipharma, for use in general anesthesia. In Europe, Paion submitted a Marketing Authorisation Application to the European Medicines Agency for procedural sedation in November 2019. In China, licensee Yichang Humanwell filed for market approval in procedural sedation in November 2018. In South Korea, licensee Hana Pharm filed for market approval in general anesthesia in December 2019.

(d) BYFAVO^{TM} Development

Paion, a wholly-owned subsidiary of Paion AG, a publicly-listed specialty pharmaceutical company headquartered in Aachen, Germany which is developing and aiming to commercialise innovative drugs to be used in out-patient and hospital-based sedation, anaesthesia and critical care services, took over the development of remimazolam as a pre-IND candidate in 2008 and advanced the development through Phase 3 trials.

The primary clinical development of BYFAVO^{TM} was completed in 2017. A programme of 22 clinical studies involving 1,731 subjects investigated the pharmacology and safety of BYFAVO^{TM} in a range of populations and its safety and efficacy in procedural sedation, general anesthesia sedation and intensive care unit sedation. Data from the clinical programme were used to support the new drug application to the FDA for induction and maintenance of procedural sedation in adults, which was approved on 2 July 2020.

The three pivotal studies included in the BYFAVO^{TM} label are described below.

Pivotal Clinical Studies

CNS7056-006. Phase 3 study in patients undergoing colonoscopy with concomitant analgesic (fentanyl), conducted in the US.

This study, now published in the literature,[61] was a double-blind, randomised comparison of BYFAVO^{TM} and placebo, with an exploratory open-label midazolam arm, as sedation for colonoscopy procedures and

[61] Rex DK, et al, 2018.

was conducted at 13 centres in the US. A total of 461 adult patients with ASA status I-III were randomised on a 30:6:10 basis to receive an initial dose of 5 mg of BYFAVO™ followed by supplemental doses of 2.5 mg as required, or identical volumes of a matching placebo, or a standard regimen of midazolam (1.75 mg initial dose and 1 mg supplemental doses, or less for elderly, debilitated or chronically ill patients). Patients received fentanyl pretreatment for analgesia, with a regimen of 50 µg to 75 µg initially and 25 µg supplemental doses every 5-10 minutes until adequate analgesia or a maximum dose of 200 µg was reached, subject to modification in elderly or disabled patients. The primary endpoint was a successful procedure, defined as completion of the procedure, no requirement for an alternative sedative medication, and no more than 5 doses of blinded study medication (BYFAVO™ or placebo) within any 15-minute window. In the midazolam arm, the requirement was no more than 3 doses in any 12-minute window. In the intent-to-treat (ITT) population, the success rate for BYFAVO™ (91.3%) was significantly superior to placebo (1.7%; $p < 0.0001$). The comparison between BYFAVO™ and midazolam was designed only to be exploratory and therefore not appropriate for formal statistical testing, but the success rate with BYFAVO™ was numerically much higher (91.3% vs 25.2%).

ITT population	**Placebo**		**BYFAVO™**		**Midazolam**	
Number of subjects	60		298		103	
Primary Endpoint: Procedure Success†	**1**	**1.7%**	**272**	**91.3%***	**26**	**25.2%**
Key Secondary Endpoints						
Median time to procedure start, mins	19.5		4.0*		19	
Mean time to fully alert from end of procedure, mins	15		7.0*		16	
Median time to discharge ready from end of procedure, mins	53		43.0*		48.0	

*$p < 0.0001$ (all versus placebo)

† Completion of the procedure, no requirement for an alternative sedative medication, and no more than 5 doses of blinded study medication within any 15-minute window (no more than 3 doses in any 12-minute window for midazolam).

The safety profile of BYFAVO™ was favourable, compared to placebo and midazolam. One or more treatment-emergent adverse events occurred in 73.6% of patients in the BYFAVO™ group, compared to 78.3% in the placebo group and 91.2% in the midazolam group. Vascular disorders, such as hypotension and hypertension, occurred in 62.2% of the BYFAVO™ group, 68.3% of the placebo group and 81.4% of the midazolam group, while cardiac disorders (primarily bradycardia and tachycardia) occurred in 17.9%, 23.3% and 25.5% of the BYFAVO™, placebo and midazolam groups, respectively. Respiratory events such as bradypnoea, hypoxia and respiratory depression were seen in 3.7%, 6.7% and 5.9% of BYFAVO™, placebo and midazolam patients, respectively. Other events generally occurred in fewer than 5% of patients in any group.

This study confirms that BYFAVO™ is effective for procedural sedation in patients undergoing colonoscopy and the Directors believe it may offer potential benefits over midazolam, especially in terms of overall procedure duration and patient recovery times.

CNS7056-008. Phase 3 study in patients undergoing bronchoscopy with concomitant analgesic (fentanyl), conducted in the US.

This study, now published in the literature,[62] was a double-blind, randomised comparison of BYFAVO™ and placebo, with an exploratory open-label midazolam arm, as sedation for bronchoscopy procedures and was conducted at 15 centres in the US. A total of 446 adult patients with ASA status I-III were randomised on a 30:6:6 basis to receive an initial dose of 5 mg of BYFAVO™ followed by supplemental doses of 2.5 mg as required, or identical volumes of a matching placebo, or a standard regimen of midazolam (1.75 mg initial dose and 1 mg supplemental doses, or less for elderly, debilitated or chronically ill patients). Patients received fentanyl pretreatment for analgesia, with a regimen of 25-50 µg initially and 25 µg supplemental doses every 5-10 minutes until adequate analgesia or a maximum dose of 200 µg was reached, subject to modification in elderly or disabled patients. The primary endpoint was a successful procedure, defined as completion of the procedure, no requirement for an alternative sedative medication, and no more than 5 doses of blinded study medication (BYFAVO™ or placebo) within any 15-minute window. In the midazolam arm, the requirement was no more than 3 doses in any 12-minute window. In the intent-to-treat

[62] Pastis NJ, et al, 2019.

(ITT) population, the success rate for BYFAVO™ (80.6%) was significantly superior to placebo (4.8%; $p < 0.0001$). Again the success rate with BYFAVO™ was numerically much higher than with midazolam (32.9%).

ITT population	**Placebo**		**BYFAVO™**		**Midazolam**	
Number of subjects	63		310		73	
Primary Endpoint: Procedure Success†	**3**	**4.8%**	**250**	**80.6%****	**24**	**32.9%**
Key Secondary Endpoints						
Median time to procedure start, mins	19		4.1**		15.5	
Median time to fully alert from end of procedure, mins	13.6		6.0**		12	
Median time to discharge ready from end of procedure, mins	81.0		60.0*		66.0	

*$p < 0.001$**$p \leq 0.0001$ (all versus placebo)
† Completion of the procedure, no requirement for an alternative sedative medication, and no more than 5 doses of blinded study medication within any 15-minute window (no more than 3 doses in any 12-minute window for midazolam).

This study confirms that BYFAVO™ is effective for procedural sedation in patients undergoing bronchoscopy and the Directors believe it may offer similar potential benefits over midazolam to those expected in colonoscopy.

CNS7056-015. Phase 3 study in more debilitated patients undergoing colonoscopy, conducted in the US.

This was primarily a safety study involving more debilitated ASA III-IV status patients undergoing colonoscopy, with fentanyl pretreatment for analgesia. In this double-blind, placebo-controlled study, with an open-label midazolam arm, 79 adult patients were randomised and 77 treated in the BYFAVO™ (N=31), placebo (N=16) and midazolam (N=30) arms. The BYFAVO™ regimen was adaptable to the status of the patient, with a starting dose of either 2.5-5 mg and supplemental doses of 1.25-2.5 mg. The safety of BYFAVO™ in this least fit patient population was comparable to that seen in the wider patient population. In the intent-to-treat (ITT) population, the procedure success rates were 84.4% for BYFAVO™, 0.0% for placebo and 12.9% for midazolam.

Pooled Safety Data from Phase 3 Clinical Studies

Across the three Phase 3 studies described above, involving 966 patients, of whom 630 received BYFAVO™, the incidence of adverse events, serious adverse events and discontinuations due to adverse events was similar between BYFAVO™, placebo and midazolam. There were no deaths.

	Placebo		**BYFAVO™**		**Midazolam**	
Number of subjects in safety population	135		630		201	
Any treatment-emergent adverse event (TEAE)	112	83.0%	514	81.6%	182	90.5%
Any TEAE judged related to study drug	52	38.5%	233	37.0%	91	45.3%
Any serious TEAE	4	3.0%	17	2.7%	1	0.5%
Any serious TEAE judged related to study drug	0		1	0.2%	0	
Any TEAE leading to discontinuation of study drug	0		1	0.2%	1	0.5%

The mean cumulative dose of BYFAVO™ was 10.91 mg (range 5-30 mg), the mean number of supplemental doses was 2.4 (range 0-10) and the mean duration from first to last dose was 10.87 minutes (range 1-49.5).

The Directors believe this confirms that BYFAVO™ has a favourable safety profile compared to midazolam, the current standard-of-care in procedural sedation.

Other Clinical Studies

A further 19 studies have been conducted on intravenous BYFAVO™. Of these, 11 were pharmacology studies, including eight pharmacokinetic, pharmacodynamic and cardiac function studies in healthy volunteers, one study each in subjects with renal and hepatic impairment and four study investigating abuse liability in otherwise healthy recreational CNS depressant users.

These pharmacology studies established that BYFAVO™ has a distribution half-life of 0.5-2 minutes and is rapidly metabolised in the liver to an inactive metabolite. The terminal half-life is not affected by renal impairment but is prolonged with increasing severity of hepatic impairment. BYFAVO™ works by binding potently and selectively to $GABA_A$ receptors in the brain and there is no evidence of any off-target receptor activity by BYFAVO™ or its metabolite. The benzodiazepine antagonist flumazenil has been shown to reverse the sedative effects of BYFAVO™ and may therefore be useful in emergency or overdose situations. BYFAVO™ has a very low potential for drug-drug interactions. In a study in recreational CNS depressant users, BYFAVO™ had a comparable abuse potential to midazolam. It has very low bioavailability when taken orally and large doses are required for any effect when taken intranasally, making these routes unattractive for potential abuse.

Two studies have investigated the effect of BYFAVO™ on the QT interval of the electrocardiogram. In study CNS7056-005, 57 subjects were randomised to a treatment sequence involving 10 and 20 mg doses of BYFAVO™, 2.5 and 7.5 mg doses of midazolam, IV placebo and oral moxifloxacin, in a standard "thorough QT study" design. This showed that both BYFAVO™ and midazolam were associated with a small increase in QTc at 30 seconds and 2 minutes after dosing. For the higher 20 mg BYFAVO™ dose, this reached 10.4 msec (90% confidence interval: 6.5-14.3 msec) at 30 seconds and declined to 6.3 msec (90% CI: 2.3-10.2 msec) at 2 minutes. Beyond 2 minutes, there was no clinically relevant effect on QT. Because a bolus dose of BYFAVO™ causes an immediate, substantial but short-lived increase in heart-rate, it was hypothesised that the increase in QTc was an artefact of the heart rate rise rather than a true effect on cardiac repolarisation. Accordingly, a follow-up study, CNS7056-017, was conducted to look specifically at the relationship between steady state plasma concentrations of remimazolam and QTc, avoiding the potentially confounding heart-rate effect seen with a bolus dose. This showed no significant effect on QTc of remimazolam plasma concentrations up to 2.0 µg/mL. There are no warnings in the BYFAVO™ label relating to QT prolongation.

In addition to the Phase 3 studies described above, another eight Phase 2-3 studies have been conducted, including two others in procedural sedation, five in general surgical anesthesia and one in intensive care unit sedation. The two procedural sedation studies, one in colonoscopy procedures (CNS7056-004), the other in upper gastrointestinal endoscopy (CNS7056-003), were both double-blind, randomised, dose-finding trials comparing BYFAVO™ with midazolam. In study CNS7056-003, efficacy of a single bolus dose of BYFAVO™ was comparable to that of midazolam but it was clear that a single bolus dose was sub-optimal and that supplemental doses would be needed, as is standard practice with midazolam. In study CNS7056-004, which introduced supplemental doses, all three dosing regimens of BYFAVO™ tested achieved more than 90% procedure success and were more effective than midazolam (75% success), the optimal BYFAVO™ regimen being 5 mg with 3 mg supplemental doses (success rate 97.5%, p=0.007 vs midazolam).

(e) BYFAVO™ commercial opportunity and commercialisation plans

The Company intends to promote BYFAVO™ into hospitals (including out-patient departments) and ambulatory surgical centres in the US for use in procedural sedation in colonoscopies and endocopies, bronchoscopies and arthroscopies, all of which are procedures where conscious sedation is preferred by physicians.[63] There were an estimated 20.2 million colonoscopies[64] and over 1.5 million bronchoscopies in the US in 2018[65]. Additional opportunities for the promotion of BYFAVO™ have been identified, including other gastrointestinal procedures, cardiac catheterisations, ophthalmic procedures, head and neck surgeries, interventional radiology, stent placements and plastic surgery.

The two sedation agents that are most commonly used for procedural sedation currently are midazolam and propofol. The pharmacodynamic profile of midazolam and the safety profile of propofol create an unmet medical need for patients that receive sedation. Important attributes of BYFAVO™ over midazolam include improved speed of recovery and reduced time to patient discharge, the speed of onset of sedation,

[63] American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018.
[64] Source: iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019.
[65] Source: iData Research, US Market Procedure Numbers for Bronchoscopy October 2019.

elimination half-life and a better safety profile. The anticipated benefits of BYFAVO™ over propofol include an improved haemodynamic impact and fewer side-effects on respiration.

The Directors believe the Group will be able to address this procedural sedation market using the same sales force, market access and medical science liaison (MSL) teams as are planned to be established for BARHEMSYS®. As with BARHEMSYS®, BYFAVO™ is expected to be part of the diagnosis-related-group (DRG) capitated payment system and, in order to be used in any hospital, it will need to be approved by the relevant Pharmacy & Therapeutics Committee (P&T) and be placed on that institution's formulary of approved drugs. It can take on average nine to twelve months to secure formulary access, meaning that initial sales volumes are not expected to be substantial.

It is intended that BYFAVO™ will be introduced at a premium price to the leading generic products midazolam and propofol and positioned as a versatile agent with a comprehensive value proposition compared to existing leading standards of care. Market research[66] indicates a wholesale acquisition price of $25 to $35 per patient procedure ought to allow good penetration of the market.

Care Settings: The primary opportunity for use of BYFAVO™ is in the outpatient setting where it is estimated that up to 25 million GI procedures alone requiring sedation are performed each year in the US.[67] This market continues to grow as more and more surgical procedures are transitioned from the inpatient to the outpatient setting. Approximately 60 per cent of gastrointestinal endoscopies occur in the ambulatory surgical centre (ASC) setting and approximately 40 per cent in the hospital outpatient department (HOPD) setting.[68]

It is planned that the Acacia Pharma sales force, market access and MSL teams will implement activities focused on securing Integrated Delivery Network (IDN) access and then promoting product use through key accounts, focusing on settings of care and patient types, for example. The proposed field deployment plan includes six regions supported by region-specific business directors, territory account managers, national account directors and medical science liaisons. All customer-facing organisations will be supported by appropriate corporate headquarter personnel.

4.3 *APD403*

(a) Chemotherapy-induced nausea and vomiting (CINV)

CINV is one of the most common and feared side effects of cancer chemotherapy.[69] In patients receiving highly emetogenic chemotherapy ("**HEC**"), such as cisplatin for lung and bladder cancers and the combination of an anthracycline and cyclophosphamide in women with breast cancer, the incidence of CINV is over 90 per cent. There are also many moderately emetogenic chemotherapy ("**MEC**") agents and regimens which can cause CINV in between 30 per cent and 90 per cent of patients. Nausea and vomiting can occur on the day of chemotherapy (acute CINV) and can persist for two to five days after chemotherapy (delayed CINV). CINV has a significant effect on quality of life and can compromise patient health. Severe CINV may necessitate a delay or reduction in chemotherapy and can ultimately lead to the withdrawal of treatment. The goal of CINV management is the prevention, rather than treatment, of symptoms.[70]

(b) Current management of CINV

Therapeutic guidelines for the management of CINV have been published by several major oncology organisations, including the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO), the Multinational Association of Supportive Care in Cancer (MASCC) and the National Comprehensive Cancer Network. Current guidelines[71] recommend the use of triple therapy, comprising a 5-HT_3 antagonist (e.g. ondansetron), a corticosteroid (e.g. dexamethasone) and an NK-1 antagonist (e.g. aprepitant, or its intravenous prodrug fosaprepitant), in patients receiving HEC. All three agents are given immediately prior to chemotherapy to prevent acute CINV and dexamethasone and oral aprepitant are given for two to four days thereafter to prevent delayed CINV. A single higher dose of

[66] TwoLabs, MKO Global Partners Prepared for Cosmo Pharmaceuticals, 2018.

[67] Director estimates based on calculations using available procedural data, applied Compound Annual Growth Rate and quantitative market research responses as follows iData Research, US Market Report Procedure Numbers for Gastrointestinal Endoscopic Devices February 2019; American Society of Anesthesiologists, Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018; and Quantitative Market Research prepared by The Link Group for Cosmo Technologies (March 2019). Please refer to Part II (Risk Factors) for additional information on the Company's estimates and risks relating thereto. See *"The Group's estimates relating to its target markets are based on certain assumptions and may be inaccurate which could result in lower than expected revenues or higher than expected costs."*

[68] Joseph DA, Meester RGS, et al. (2016). Colorectal cancer screening: estimated future colonoscopy need and current volume and capacity. Cancer. 122(16); SG2. Market Landscape and Segmentation Report prepared for Acacia Pharma.

[69] Edison analyst note on Tesaro, February 2013, page 12.

[70] Roila et al., 2016. NCCN Guidelines 2017.

[71] Basch et al., 2011, pages 4189 to 4198.

intravenous fosaprepitant on day one has been shown to be as effective as three daily doses of oral aprepitant. For patients receiving MEC, the guidelines recommend the use of the 5-HT_3 antagonist palonosetron in combination with a corticosteroid. For patients who still suffer CINV despite receiving prophylaxis, guidelines recommend consideration of dopamine D2 receptor antagonists as rescue therapy.

The use of three-drug prophylaxis can control acute CINV in 80 to 90 per cent of patients receiving HEC.[72] However, control of delayed CINV is much less satisfactory, with failure occurring in 30 to 50 per cent of patients, primarily due to nausea rather than vomiting.[73] Therefore, the Directors consider management of nausea in the delayed phase of CINV to be a major unmet medical need.

A number of studies have demonstrated benefits for the dopamine antagonists metopimazine and olanzapine in delayed CINV. However, these drugs are not approved for the management of CINV and have side effects which could limit their use.[74] In contrast, based on the results of the studies to date, APD403 has a favourable safety profile and data generated by the Group indicate that APD403 could improve outcomes in delayed CINV without compromising patient safety.

(c) Competitive products

The Directors are aware of two products that was approved and launched in early 2018 for the management of CINV in recent years, both by Heron Therapeutics Inc: SUSTOL®, a new formulation of the existing 5-HT_3 antagonist granisetron; and CINVANTI®, an alternative formulation of the NK-1 antagonist fosaprepitant, which is already marketed by Merck as Ivemend®, and which it competes directly with and can be substituted for.

The Directors are aware of the development by Starton Therapeutics Inc of a transdermal patch of the dopamine antagonist olanzapine for PARP inhibitor induced nausea and believe the product has undergone preclinical testing but late-stage clinical studies have yet to start.

(d) APD403 product description

APD403 is a product candidate for the management of CINV comprising the dopamine antagonist amisulpride, the same active ingredient in BARHEMSYS®. Amisulpride has never been submitted for approval in the US but has been approved in approximately 50 countries in Europe and elsewhere in the world. The Group anticipates that APD403 will be given as an intravenous injection immediately before cancer patients receive their emetogenic chemotherapy to prevent acute CINV, and as an oral tablet to take at home for three days subsequent to prevent delayed CINV. Therefore, in those countries where amisulpride is available for other uses, APD403 will be differentiated from the existing marketed products by route of administration and dose.

The Group's rationale for investigating amisulpride for the management of PONV is described in Section 4.1(e) of this Part VI (*Information on the Company and the Group*). As dopamine antagonists have historically been effective at managing nausea, the main unmet need in CINV, but have not been included in CINV prophylaxis standard of care regimens, the potential for amisulpride to improve the management of CINV was considered. The pre-clinical emesis studies referred to in section 4.1(f) indicated that amisulpride could indeed have utility in CINV. This pre-clinical antiemetic effect has now been confirmed in clinical studies in cancer patients. The Group has filed patent applications describing the new use of amisulpride for the management of CINV in major pharmaceutical territories. These applications have been granted in key pharmaceutical territories such as the US and Europe.

(e) APD403 Development Status

APD403 has been evaluated in two clinical studies.

DN10007. Open-label Phase 2a proof-of-concept study.

This study, now published in the literature,[75] was an open-label, non-randomised, ascending dose Phase 2a study, conducted in three centres in Denmark and one in the UK and designed to establish clinical proof of concept of APD403 as an antiemetic in cancer patients receiving the HEC agent cisplatin at a dose of at least 50 mg/m^2. The primary endpoint of the study was complete response in the acute phase of CINV, defined as the absence of emesis and no requirement for rescue antiemetic therapy in the 24 hours after chemotherapy; occurrence of nausea was recorded as a secondary endpoint. A single dose of APD403 was

[72] Poli-Bigelli et al., 2003, pages 3090 to 3098; Hesketh et al., 2003, pages 4112 to 4119.
[73] Warr et al., 2005, pages 2822 to 2830.
[74] Herrstedt et al., 1997; Navari et al., 2016.
[75] Herrstedt et al., 2017.

given to 28 subjects just prior to cisplatin chemotherapy at the dose levels 2.5 mg (five subjects), 7.5 mg (five subjects) and 20 mg (18 subjects). Although there were no complete responses at the 2.5 or 7.5 mg dose levels, two complete responses were seen in the cohort receiving 20 mg amisulpride and a noteworthy absence of nausea was also reported. As a result, it was decided to recruit a further cohort of 23 subjects to receive 20 mg APD403 in combination with a standard intravenous dose of ondansetron. In that cohort, 19 subjects (83 per cent) had a complete response. Very little nausea was seen in the cohort and no significant side effects were reported.

The Directors believe this study shows that APD403 at 20 mg, when combined with a standard dose of intravenous ondansetron, is well tolerated and effective at preventing nausea and vomiting in the first 24 hours after cisplatin chemotherapy and proves in principle that APD403 could be a useful antiemetic in patients receiving chemotherapy.

DN10016. Phase 2, dose ranging study in delayed CINV completed March 2015.

This was a randomised, double-blind, dose-ranging Phase 2 study, now published in the literature,[76] conducted in 25 centres in the UK, Denmark and Germany, involving 328 cancer patients receiving HEC (either cisplatin at a dose of 70 mg/m^2 or greater or a combination of an anthracycline and cyclophosphamide for breast cancer). The primary objective was to characterise the dose response of APD403 in the delayed phase of CINV. Patients were randomised to receive a placebo or one of three doses of APD403 (10, 20 or 40 mg) orally on days 2, 3 and 4 after chemotherapy, having received the same acute-phase antiemetic prophylaxis of intravenous ondansetron plus 20 mg of intravenous amisulpride immediately before chemotherapy.

One-fifth of the study population was randomised to a "positive control" group which received the three-drug prophylactic regimen recommended by major oncology organisations such as ASCO and ESMO, comprising intravenous ondansetron, dexamethasone and fosaprepitant prior to chemotherapy followed by oral dexamethasone on days two, three and four. This group was intended as a useful efficacy benchmark, as the response rate in such a mixed population was difficult to predict from historical data in the literature; formal statistical testing against the APD403 groups was not planned. The primary endpoint was delayed phase complete response, defined as no vomiting or retching and no requirement for antiemetic rescue medication in the period 24-120 hours after the administration of chemotherapy.

In the per-protocol population, APD403 at 10 mg was significantly superior to placebo in terms of delayed phase complete response (46 per cent vs. 20 per cent, p=0.006 after adjustment for multiplicity). Complete response in the overall phase (0-120 hours) was also significantly improved by APD403 (36 per cent vs 17 per cent, p=0.015). Nausea occurred in the 24-120-hour period in 82 per cent of patients in the placebo group compared to 63 per cent in the APD403 10 mg group (p=0.025); and 63 per cent of the placebo group had delayed phase emesis compared to 46 per cent in the APD403 10 mg group (p=0.040). As expected, the two-antiemetic experimental regimens were not as effective as the three-antiemetic "benchmark"; however, the difference in delayed and overall efficacy was no more than would be predicted given the additional antiemetic, amounting to a 13 percentage point difference in delayed phase complete response and 17 percentage points in overall phase complete response. In terms of nausea there was very little difference between the two groups: in the benchmark group, 65 per cent of patients had nausea at some time in the 0-120-hour period compared to 69 per cent in the APD403 10 mg group. The greatest difference between the benchmark and APD403 groups was efficacy in the acute phase, with 75 per cent of the three-drug benchmark group achieving complete response compared to 47 per cent across the four groups which received only APD403 and ondansetron, illustrating the benefit of the additional IV antiemetic given prior to chemotherapy. This difference mirrored results seen in published trials when an NK1-antagonist was added to ondansetron plus dexamethasone. Because delayed phase response has been shown to be strongly associated with acute phase response, a sub-analysis of outcomes in the subset of patients achieving complete response in the acute phase was pre-planned. In this key subset, the incidence of delayed phase complete response in the APD403 10 mg group (75 per cent) was similar to that in the benchmark group (70 per cent) and significantly better than that in the placebo group (44 per cent, p=0.022). The benefit in terms of absence of nausea was especially marked: 68 per cent for APD403 10 mg, 28 per cent for placebo (p=0.009) and 55 per cent for the benchmark. Rates of no emesis and no use of rescue medication were similar for the APD403 10 mg and benchmark groups; the superiority over placebo did not reach significance.

[76] Herrstedt et al., 2018.

	Placebo	Amisulpride 10 mg	Amisulpride 20 mg	Amisulpride 40 mg
Number of subjects	65	59	67	64
Primary Endpoint Complete Response in delayed phase†	13 (20.0%)	27 (45.8%)**	21 (31.3%)	20 (31.3%)
Secondary endpoints				
Complete Response overall (0-120 h)	11 (16.9%)	21 (35.6%)*	17 (25.4%)	17 (26.6%)
Vomiting/retching (24-120 h)	41 (63.1%)	27 (45.8%)*	37 (55.2%)	37 (57.8%)
Nausea† (24-120 h)	53 (81.5%)	37 (62.7%)*	47 (70.1%)	47 (73.4%)

*p≤0.05**p≤0.01 (two-sided p values)
† No emesis or use of rescue medication in 24-120 hours after chemotherapy
‡VAS score > 5 mm

The data obtained to date have led the Directors to infer that oral APD403 at 10 mg a day may be as effective as dexamethasone in the delayed phase of CINV and could therefore add significantly to the current standard of care. The 20 mg and 40 mg doses of APD403 were generally better than placebo but not as efficacious as 10 mg, which is consistent with previous results showing a "bell-shaped" dose-response for the product. No significant differences were seen in adverse events, vital signs or laboratory parameters between any of the APD403 groups and placebo, except for a modest, dose-dependent increase in mean prolactin levels after treatment. The Directors believe this study shows that APD403 at 10 mg on days two to four after HEC is safe and effective at preventing delayed phase CINV and supports further study of APD403 in CINV.

In a Type C regulatory meeting in April 2019 the FDA indicated that this trial could potentially be acceptable as one of the two registrational trials needed to support an APD403 filing in CINV.

(f) APD403 regulatory path to approval

A commercially viable tablet formulation has been developed and it is planned to manufacture batches for regulatory stability and clinical trial use within 36 months. Positive data from one further pivotal study is expected to be sufficient to secure the target APD403 label of prevention of nausea and vomiting associated with chemotherapy, including but not limited to highly emetogenic chemotherapy. The details of the required Phase 3 study were agreed with the FDA in April 2019. Subject to the successful launches of BARHEMSYS® and BYFAVO™, the study is expected to commence in 2021 and take up to 2 years to complete, enabling a potential supplemental NDA submission in late 2022 or early 2023.

(g) APD403 commercial opportunity

Approximately 6.6 million doses of 5-HT_3 antagonists were administered on the first day of chemotherapy in the US in 2011. Approximately four million of these were used for the management of CINV associated with HEC.[77] Worldwide therapeutic guidelines recommend "triple therapy" comprising a 5-HT_3 antagonist (e.g. ondansetron), a corticosteroid (e.g. dexamethasone) and an NK-1 antagonist (e.g. aprepitant, rolapitant) as the standard of care for CINV in "all" patients receiving HEC and "appropriate" patients receiving MEC. The Therapeutic Guidelines further clarify that the "appropriate" definition of MEC includes carboplatin-containing regimens, such as those used for breast cancer treatment.[78] Therefore, the Group estimates that the number of chemotherapy regimens for which "triple therapy" CINV prophylaxis is appropriate is approximately five million per annum in the US.

The two most widely prescribed injectable branded antiemetics for CINV are CINVANTI® (IV aprepitant) and Emend®/Ivemend® (aprepitant/fosaprepitant), both NK-1 antagonists. Typical prices for branded antiemetics in CINV have been in the range of $250-500 per cycle. Among recent branded products in the space, Merck and Co. reported global 2018 sales of Emend® of $522 million. Aloxi® net sales in FY2016 were $412 million in the US. These products are now off-patent and prices are reducing, freeing up potential budget for new branded entrants. Heron Therapeutics reported CINVANTI® net sales in FY 2019 were $132 million in the US in its second year on the market.

[77] Morgan Stanley analyst note on Tesaro, 2012, Deutsche Bank analyst note on Tesaro, 2013, Edison analyst note on Tesaro, 2014, NCCN Guidelines for antiemesis, 2017.
[78] Roila et al., 2016.

Reimbursement for CINV therapies can vary dependent upon product form and patient type (e.g. Medicare vs. private pay insurance).[79] The majority of US cancer patients are covered by Medicare.[80] In this population, most products administered in physician offices and hospital out-patient settings are reimbursed at ASP plus six per cent.[81] Reimbursement among private pay insurers varies widely across products and is often negotiated with each manufacturer.

Market research involving over 250 community and hospital-based oncologists was commissioned by the Group in Q3 2015 to assess physicians' initial reaction to a target product profile for APD403 in line with the results from the Phase 2 dose ranging study. Based upon a product profile describing only the results of a single Phase 3 HEC study, these oncologists indicated that they expect to use APD403 in approximately 45 per cent of HEC patients and 34 per cent of MEC patients, and further indicated that over 80 per cent of the use of APD403 would be in combination with the physician's current standard of care.

The Directors believe that, should the remaining Phase 3 study confirm the initial results for APD403 and support approval of the product, the drug would be sold at a price similar to that of recent branded products and it is likely to be used in those patients currently recommended in the guidelines to receive "triple therapy". The Group would promote APD403 for use in combination with the current standard of care treatments to improve response rates. To support the launch of APD403 in the US, the Group plans to moderately expand and leverage the commercial operation initially focused on BARHEMSYS® and BYFAVO™ with marketing and sales professionals that have extensive oncology and/or CINV experience.

5. Commercialisation Strategy And Operations

5.1 *Overview*

The Group intends to commercialise its products predominantly directly in the US. In the case of BARHEMSYS® and APD403 and where commercially viable and regulatory approvals are obtained and for which any necessary consents are obtained to do so, the Group may also establish licensing and/or distribution agreements with selected pharmaceutical partners outside the US, such as in Europe. Products such as BARHEMSYS® and BYFAVO™ are prescribed by hospital-based specialist physicians, such as anaesthetists (including in hospital out-patient departments), provided the product is on approved formulary lists at the relevant hospital. The Directors believe that a focused US sales force targeting anaesthetists and their surgical teams will be an appropriate approach to marketing of BARHEMSYS® and BYFAVO™ in the US. The US infrastructure established for BARHEMSYS® and BYFAVO™ could be moderately increased to accommodate APD403 once approved and other complementary products that may be identified.

The recent impact of the COVID-19 pandemic on the US healthcare system, and in particular hospitals and surgical centres, has been well publicised. Whilst the situation has created certain challenges in accessing decision makers in hospitals and ambiguity around the timing for the resumption of their formulary committee meetings, the COVID-19 situation has created potential opportunities for the Group as it has led to drug shortages for the most commonly used procedural sedatives like midazolam and propofol as well as antiemetics like ondansetron and dexamethasone, all of which are currently on the FDA drug shortages list. It has also created procedural backlogs and potential pent up demand for the launch of the Group's products as hospitals and surgical centers now need to significantly increase their patient throughput, which has further heightened the value proposition for both drugs in order to regain lost profits.

The situation has caused the Group to adjust its commercialisation strategy to accommodate more virtual engagements with clinical staff and further reinforces the need for the Group to recruit and retain experienced representatives with longstanding key customer relationships to facilitate dialogue even with restricted physical access to the facility. Furthermore, due to the increasing virtual engagement with hospital accounts, the Directors believe the sales representatives can increase their customer reach, thereby enabling the sales team to become even more productive and able to address a greater number of customers and accounts than previously envisaged.

For a discussion of the risks related to the Group's commercialisation strategy see Part II (*Risk Factors*).

[79] The Patient Protection and Affordable Care Act, 2010, 42 C.F.R. § 405.
[80] Kantar Health, page 2, Figure 2.
[81] ASPE, June 2014.

5.2 *Commercialisation strategy and operations in the US*

US healthcare financing and the reimbursement system

A goal of healthcare providers and payors in the US is to manage patient throughput in hospitals and clinics efficiently and minimise costs, whilst providing patients with good medical care and a positive experience. Much of the cost of US healthcare is financed through private health insurance and government funded programmes such as Medicare and Medicaid. The Medicare system includes restrictions on the procedures and products that will be funded and the rates at which hospitals and physicians will be reimbursed for delivery thereof. Similarly, private insurers set reimbursement policies. Where hospitals deliver an in-patient medical procedure, they typically receive a fixed rate of reimbursement as designated by the diagnosis related group (DRG) from Medicare or the relevant private insurance system regardless of the amount or type of drugs or other products used for the procedure and the length of stay in the hospital, and each hospital seeks to optimise its own finances through the establishment of a formulary committee which considers which products should be used, having regard to efficacy, safety, patient outcomes, cost and hospital efficiencies. The Group intends to seek to maximise the adoption of BARHEMSYS® and BYFAVO™ by initially focusing on promoting the inclusion of the product to these hospital formulary committees and then expanding its adoption and utilisation through targeted sales and marketing programmes.

Access and adoption

Before physicians can prescribe a drug in the hospital, the drug must generally first be placed on the hospital's list of approved products, known as a formulary. When evaluating a product for formulary inclusion, hospitals evaluate the product's safety, efficacy, cost and reimbursement, as well as the expected savings and overall impact on cost-effectiveness and quality of care compared to existing practice. The formulary adoption process for new drugs in the hospital setting typically takes nine to 12 months to gain approval. The Directors believe that formulary adoption is a critical component of commercial success for BARHEMSYS® and BYFAVO™ and growth in revenues is likely to correlate with the rate of formulary adoption. Formulary adoption will be driven by a number of factors, including the safety and efficacy of the drug, its pricing and the pharmacoeconomic benefits of its use.

Commercialisation plans

Based upon members of the Group's management team and Board's recent success in previous roles in commercialising the branded post-operative pain product OFIRMEV® in the US within a generic market, promoting a similar value proposition to that proposed for BARHEMSYS® and BYFAVO™ (efficient throughput of post-operative patients and improving the patient's surgical experience) to the same key customers (anaesthetists, surgical teams, and directors of pharmacy), the Group intends to seek to maximise the adoption of BARHEMSYS® by initially focusing on promoting the inclusion of the product on hospital formularies for use in rescue treatment of patients who have received the current standard of care prophylaxis regimen and failed. Based upon market research commissioned by the Group, this is where the greatest need currently exists (as evidenced by the current practice of re-dosing a medication, ondansetron, for rescue when the prescribing information for the drug clearly states that this is not an effective strategy). BARHEMSYS® is the first and only drug to be approved for rescue treatment of patients who have failed antiemetic prophylaxis as it has been demonstrated to be a safe and effective option that also provides pharmacoeconomic benefits with regard to patient throughput. The Directors therefore believe that a focus on rescue treatment at launch will provide the most successful path toward formulary and market adoption. Initially, the Group's commercial team will focus on promoting the drug to anaesthetists and their surgical teams for the approximately 16 million patients that fail antiemetic prophylaxis treatment each year. Once clinicians have had positive clinical experience successfully using the drug in rescue treatment, the Group plans to expand promotion of BARHEMSYS® for prophylaxis in those approximately 18 million patients per year at higher risk for PONV.

Furthermore, the Group intends to maximise the adoption of BYFAVO™ by focusing its promotional efforts on the anesthesia providers they will already be calling on for BARHEMSYS®. Anesthesia providers administer the sedation in more than 80 per cent of the gastrointestinal procedures requiring sedation in the US. These providers work across various settings (inpatient, outpatient, and ambulatory) and will be instrumental in advocating the inclusion of the drug on the formulary as well as using it across settings and the various other procedures requiring procedural sedation (such as interventional radiology procedures, ophthalmic surgeries). Highlighting to physicians the efficacy and safety of the drug, along with the potential to increase patient throughput will be key to early formulary adoption and use.

Hospital P&T Committees are usually made up of the heads of service lines throughout the hospital and the director of pharmacy. For the review of both BARHEMSYS® and BYFAVO™, the key decision makers on the committee are expected to be the members representing anaesthesia, key surgeons, and pharmacy. The Directors believe it is important to identify and work with these key decision makers by providing the clinical and pharmacoeconomic data needed to enable them to make an appropriate and informed decision. To identify, access and educate these key individuals, the Directors further believe it will be important to employ experienced local sales representatives with deep institutional knowledge and relationships in the target hospitals, partnered with experienced and knowledgeable institutional account executives and field medical team members. The hospital formulary review process is typically initiated after launch and involves numerous steps. As a result, the Group expects the average time to formulary approval for targeted accounts to be approximately nine to 12 months after launch.[82] Most accounts also require an additional period of time (approximately three months) to codify and implement the formulary approval. The Directors believe the Group can effectively launch and drive adoption of BARHEMSYS® and BYFAVO™ with the following key initiatives:

- building a sales force, institutional account executive team and field medical team with extensive hospital launch experience and strong relationships with targeted institutions;
- providing hospital and surgical centre customers with data and information supporting the cost effectiveness of BARHEMSYS® and BYFAVO™ and their impact on overall quality of care; and
- partnering with hospitals and surgical centres to focus utilisation of BARHEMSYS® and BYFAVO™ in those patients most likely to derive clinical benefit.

The Group's planned sales and marketing infrastructure

Acacia Pharma Inc., an indirectly wholly owned subsidiary of the Company incorporated in 2015 is the entity employing the commercial team. Acacia Pharma, Inc. currently employs 33 of the Group's 37 employees covering the following functions: marketing, sales management, commercial operations, national accounts, human resources, regulatory and medical communications. Acacia Pharma Inc. entered into a 5-year lease for office facilities in Indiana in Q4 2018 and intends to hire further key staff as further described in sections 2.3, 3.2 and 5.2 of this Part VI (*Information on the Company and the Group*).

The Directors have established a core commercial and medical affairs organisation based in Indianapolis to support the planned US product launches of BARHEMSYS® and BYFAVO™. The Directors believe that the Group can successfully promote its products with a focused sales force targeting the relatively small number of hospitals that account for a substantial portion of the prescribing activity. An estimated 88 per cent of the most commonly used IV antiemetics (ondansetron and dexamethasone) are purchased by hospitals. Approximately 1,600 hospitals perform nearly 80 per cent of hospital-based surgical procedures.[83] Given the limited number of centres, the Group plans to build a sales force of initially 30 sales representatives initially focused on anaesthetists and surgical teams in these institutions in order to build formulary access, growing the number of sales representatives as product demand grows to approximately 60 over 3 years. Each of the initial 30 sales representatives is expected to have its own sales territory covering accounts with greatest immediate opportunity. To support the launch of APD403, the Group plans to expand the sales force by approximately 40 representatives and extend promotion to the leading oncology clinics in the US. Approximately 600 oncology clinics account for over 90 per cent of the sales volume for the top prescribed antiemetics for CINV sales to clinics annually.[84] The design of the team is one vice president of sales, one national accounts group leader, one national medical science liaison leader, and six sales regions each with one regional business director, one medical science liaison, one national account director, and five territory managers.

Current status of US operations

The Group has put in place the commercial leadership team in the US with over 28 years' average industry experience of over 60 launches and recruited a number of key supporting staff. The Group has sought, and will continue to seek, to employ highly experienced professionals who understand the intricacies of promoting a branded product in a generic market to key customers (anaesthetists, surgeons, surgical support teams, and pharmacy). The key workstreams recently completed in preparation for launch include: refining the account targeting and optimising the sales force deployment, incorporating additional market research study findings into the promotional messaging, identifying and working with key opinion leaders to help

[82] P&T committee approval timing based upon management experience and TwoLabs/MKO US Pricing and Market Access Research, January 2019.
[83] Acacia Pharma Preliminary US BARHEMSYS® Sales and Marketing Plan, November 2014.
[84] Heron, Intrinsiq data from July 2012 to July 2013.

educate and prepare the market, preparing and testing the pharmacoeconomic data and the budget impact model to support product use, developing promotional materials to be used at launch by the sales force, and developing the sales training materials needed for successfully launching the product. The senior commercial team is continuing to monitor the COVID-19 impact on hospitals and surgical centres and is planning the launch timing to coincide with a return to more normalised surgical volumes and has already identified and recruited experienced hospital sales professionals to be hired shortly before launch. In the interim, the current field team consisting of sales leadership (with 22 years' average industry experience and over 18 years of hospital experience), national accounts directors (with 24 years' average industry experience and over 21 years of hospital experience), and medical science liaisons (with 22 years' average industry experience and over 10 years as a medical science liaison) have been working to begin identifying early adopting accounts and begin the formulary adoption process wherever possible.

5.3 *Commercialisation Strategy outside the US*

In markets outside the US, such as Europe, the Group intends to establish licensing and/or distribution agreements where possible with selected pharmaceutical partners where appropriate and commercially viable and regulatory approvals are obtained and for which any necessary consents are obtained.

6. Regulatory Overview

Prior to marketing a medicinal product, a new drug approval or marketing authorisation (also commonly known as a product licence) must be obtained. Government authorities in the US, Europe and most other jurisdictions where the Group intends to distribute its licensed products extensively regulate, among other things, the research, development, clinical testing, manufacture, approval, distribution, marketing and post-marketing surveillance of pharmaceutical product candidates. Obtaining regulatory approvals and ensuring subsequent compliance with applicable laws and regulations can be a lengthy process involving substantial financial and managerial resources. Regulatory requirements and procedures vary from jurisdiction to jurisdiction and the timing and success of efforts to obtain regulatory approvals can be highly uncertain. Development of a successful product candidate, from identification, through pre-clinical testing and clinical studies, to registration, can take more than ten years.

The regulatory body managing the approval and use of medicines in the US is the Food and Drug Administration (FDA). The FDA is a consumer protection agency which protects the public from unsafe foods, drugs, medical devices, cosmetics, and other potential hazards. It also protects the rights and safety of patients in clinical trials of new medical products, monitors the promotional activities of drug and device manufacturers, regulates the labelling of all packaged foods, and monitors the safety of the nation's blood supply. In assessing an NDA, the FDA undertakes its closest scrutiny of all during the drug approval process. Its principal goal during review is to determine whether the benefits of the new drug outweigh the risks. To reach this determination, the FDA examines the documentation provided by the sponsor and looks at samples of the drug. The FDA itself does not do research for a new medical product. Instead, it evaluates the results of studies undertaken by the manufacturer. If inadequacies are discovered in the NDA, the FDA may require additional information, further testing, or modified labelling. In cases where it is difficult to establish clearly whether the benefits of the drug outweigh the risks, a panel of outside experts is often consulted. If the FDA approves the drug, the sponsor may begin manufacturing and marketing the drug immediately. The FDA does not stop monitoring a drug once it has been marketed. It continues to evaluate the drug's safety and effectiveness through its program of post market surveillance. This program can consist of surveys, the testing of product samples, and the analysis of reported adverse reactions.

A typical FDA development programme includes requirements to conduct pre-clinical studies to evaluate a product candidate's safety profile through laboratory and in-vitro testing, followed by a series of clinical studies: first, Phase 1 studies where healthy volunteers are exposed to the product candidate in a highly controlled setting to establish safe dosing limits; followed by Phase 2 studies, where a product candidate is investigated with patients suffering from the target disease or condition, to investigate preliminary evidence of efficacy; and then Phase 3 studies which are specifically intended to provide adequate evidence of effectiveness and to establish the benefit to risk ratio to support an application for marketing approval.

6.1 *Regulation of a New Drug*

Detailed procedures involved in obtaining approval for a new drug vary from one jurisdiction to another, but a substantial degree of harmonisation has been achieved between the US, Europe and Japan as a result of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("**ICH**"). In general, it is necessary to submit a dossier including all

manufacturing, pre-clinical and clinical data to support the application. Two adequate, well controlled trials are generally needed as evidence of effectiveness in a particular indication, though where an indication is closely related to one already approved for that product, a single trial may suffice. In most cases, broadly the same dossier can be used to support a licensing application in multiple territories, such as an NDA in the US and a marketing authorisation application in Europe.

Once the licensing application is submitted, the FDA (in the US) or other regulatory authority may require further information before accepting the application. Once an application is accepted, the regulatory authority will undertake a formal review process, the timing of which will vary by jurisdiction. In the US, the FDA aims to review and determine at least 90 per cent of NDAs for standard drugs no later than 10 months after the applications are accepted for filing.[85] The review process may be extended by the regulatory authority's requests for additional information or clarification. Following the review process, the regulatory authority may grant the approval as requested, may deny approval, may grant a narrower approval than that sought, or as a condition of approval may impose restrictions that could potentially affect the commercial success of a drug or require post-approval commitments (such as post-marketing studies). Once approved, products are subject to continuing regulation and, if ongoing regulatory requirements are not met or if safety problems occur after the product reaches the market, the regulatory authority could potentially withdraw or amend the product approval, require changes in indications or labelling, or require additional clinical trials or post-marketing studies.

6.2 *Regulatory Procedures for Repurposed Drugs*

Some of the research and development steps described above may not be required with a repurposed drug as regulatory authorities may allow companies to rely upon appropriate, pre-existing information, including data published in scientific literature. Typically, doing so may reduce the amount of pre-clinical and Phase 1 testing required, as the known safety profile may be sufficient to support human efficacy testing without the need for much or any additional work, which can allow a more rapid clinical proof of concept. In addition, the scale of Phase 2 and Phase 3 testing may be capable of reduction, as pre-existing safety data may be used to supplement the clinical programme.

For example, section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (generally known as the "505(b)(2) pathway") in the US and Article 10a of Directive 2001/83/EC in Europe provide for the use of pre-existing data published on a compound. This can be useful for a repurposed drug, as it can enable a reduction in the size of the safety database that has to be generated in the clinical programme and may obviate or reduce the need for pre-clinical, clinical pharmacology, dose-ranging or other supportive data.

7. Development and Manufacturing Operations

The Group currently operates an outsourced business model managed by an experienced in-house team partnering with external organisations. The Group therefore has the flexibility to apply resources to specific projects as needs arise and adapt those resources as projects progress and evolve. The Group intends to continue to outsource a significant part of its discovery and development work as well as outsourcing the manufacture of its products to third party contract manufacturers. The Directors are seeking to identify a number of alternative suitable manufacturers in order to reduce the risk of reliance on sole-source suppliers.

The manufacturing process for BARHEMSYS® is uncomplicated, the product consisting of a buffered aqueous solution of the active ingredient, amisulpride, in a single-use, in a terminally sterilised glass vial. A commercial manufacturing partner has been qualified and full-scale commercial batches have been manufactured, labelled and packaged. The cost to manufacture BARHEMSYS® is estimated by the Directors to be less than 10 per cent of the proposed sales price. The product has a 60-month shelf life at room temperature. The Group has accumulated and stores a substantial inventory of BARHEMSYS® to minimize any supply risk.

BYFAVO™ is manufactured as a lyophilised powder and supplied in single-use glass vials. A commercial manufacturing partner has been qualified and full-scale commercial batches have been manufactured. Stability data support a 48-month shelf life at room temperature. The Directors expect that gross margins on the sale of BYFAVO™ to be typical of margins across the pharmaceutical industry.

The Group's plans assume continued fostering of manufacturing and supply chain partnerships to maximise the quality and reliability of supply for its products. The Group will scale manufacturing of its existing products once commercialisation is underway.

[85] FDA: PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017.

Key third party contractors used to date include:

(a) Sequani Limited, Cyprotex Discovery Ltd and Porsolt Partners SA for pre-clinical pharmacology and toxicology services;

(b) Premier Research Group Ltd, Quotient Clinical Limited, SynteractHCR Deutschland GmBH, Syne Qua Non Ltd, Quanticate International Ltd, Diamond Pharma Services Ltd, PRA Health Sciences Inc., Quantics Biostatistics, Richmond Pharmacology Ltd and Parexel International Ltd for clinical operation services, such as clinical trial site initiation and monitoring, data management, statistical analysis, bioanalysis and pharmacovigilance;

(c) Envigo Ltd, Strategic Bioscience Corporation Inc. and Onix Life Sciences Ltd and Extedo Inc. for regulatory services, such as the filing of clinical trial authorisation requests, Investigational New Drug submissions, the NDA and periodic drug safety updates with national regulatory authorities;

(d) Icrom, Cosma SpA, Thermo Fisher Scientific Inc., Aesica Formulation Development Ltd and Quay Pharmaceuticals Ltd for active pharmaceutical ingredient supply and formulation development and manufacture of medicinal products for clinical trial and commercial use; and

(e) for BYFAVO™, key contractors include Paion, Cambrex Corporation, Thermo Fisher Scentific Inc and Cosmo.

On 24 July 2020, the FDA approved of a second supplier for the API for BARHEMSYS® (amisulpride injection), Cosma SpA.

At the date of this Prospectus, the Group employs 37 full-time employees expected to increase to approximately 80 following the full launch of BARHEMSYS® and BYFAVO™ and recruitment of the initial planned 30 field sales representatives. If BARHEMSYS® and BYFAVO™ are successful, the Group expects to expand its sales and marketing infrastructure after launch and further to support the launch of APD403 (assuming it proceeds to commercialisation).

8. Future Funding Requirements

The net proceeds of the Fundraising, together with the Group's existing cash resources and loan facilities, are expected to allow the Group to complete the establishment of its sales and marketing infrastructure to launch BARHEMSYS® and BYFAVO™ to the hospital market in the US in late-2020 and to promote the products until the fourth quarter of 2021. See Section 3 (*Reasons for the Fundraising and Use of Proceeds*) of Part XII (*Details of the Fundraising*) of this document.

As described in the 2020 Interim Financial Statements (which are incorporated by reference into this document as set out in Part XI (*Historical Financial Information*) of this document), based on the Directors' current forecasts and plans, which assume the recruitment of a salesforce and the successful commercialisation of BARHEMSYS® and BYFAVO™ and considering the Company's existing cash and debt facilities and the net proceeds of the Fundraising, the Company has sufficient funding to continue its operations until the fourth quarter of 2021 such that, during the fourth quarter of 2021, the Company will need to raise additional funding in order to meet its cash requirements for the subsequent periods. In particular, the Company will require additional capital in order to:

(a) continue its commercialisation of BARHEMSYS® and BYFAVO™ from the fourth quarter of 2021 onwards;

(b) increase the planned expansion of its field sales force to 60 representatives if demand so justifies;

(c) explore additional, general anaesthesia endpoints for BYFAVO™;

(d) repay or service debt obligations as they become due from the fourth quarter of 2021 onwards; and

(e) recruit and complete the Phase 3 study of APD403 in CINV and launch the product.

As a result, the Company may: (i) implement further issues of Ordinary Shares; (ii) obtain additional debt financing or otherwise restructure its existing debt; and/or (iii) defer certain of its proposed strategies until such funding has been obtained, in order to enable the Company and the Group to continue as a going concern from the fourth quarter of 2021 onwards.

Nothing in this Section should be taken as limiting the working capital statement in Section 16 of Part XIV (*Additional Information*) of this document since the activities and spending requirements referred to in Section 8(a) to (e) above are not required to occur during the period of 12 months from the date of publication of this Prospectus.

9. Intellectual Property

9.1 *Summary of the Group's Intellectual Property Portfolio*

The Group has a number of patents and has filed patent applications in various jurisdictions relating to BARHEMSYS® and APD403. These patents relate to a "new use" of a known drug. Through the BYFAVO™ Assignment Agreement which became effective on 7 August 2020, the Group has acquired rights to the US patents for BYFAVO™, including a substance-of-matter patent and formulation patents. The Group is also the proprietor of registered trademarks in the UK, European Community and the US in respect of certain marks.

9.2 *Patents*

(a) Background

A patent is a right registered on a national basis, enforceable by its registered owner, to prevent others commercially practising the invention which is the subject of the patent. The intention underlying the grant of patents is to reward and encourage technological innovation. The grant of a patent does not, however, guarantee that the registered proprietor has the right to exploit the invention subject to the patent. For example, a third party may have patent rights in the same area of technology. See Part II: *"Risk Factors-Legal and Regulatory Risks– Third parties may initiate legal proceedings alleging that the Group is infringing their intellectual property rights, the outcome of which may be uncertain and could have a material adverse effect on the Group's business and prospects".*

The invention to which any patent relates must be clearly and completely disclosed in the specification set out in the patent as granted and meet the requirements for patentability established by legislation in the country in which the patent is granted.

The precise criteria of patentability differ in detail from country to country but enjoy a large measure of harmonisation as a result of a number of international treaties such as the European Patent Convention (the "**EPC**").

Although there are different routes to patent protection, in order to seek protection on an international scale in the most efficient manner, the Group files patent applications under the Patent Co-operation Treaty ("**PCT**"), which can be entered for examination by the patent office in any of the countries that are signatories to the PCT (currently 152 countries). Once filed, a PCT application is searched by a designated International Searching Authority which, in the case of the Group's applications, will be the European Patent Office ("**EPO**"). On request, a Patent Office Examiner conducts an international preliminary examination, which acts as an initial patent examination in the various designated countries. The international application then fragments into a series of national patent applications (or regional patent applications, such as in the case of a European patent application), which themselves enter the relevant national and regional examination processes towards grant. After the international phase of a PCT application is over, a "family" of related patent applications for the same invention arises for examination before the patent authorities of the chosen countries or regions.

The patent examination process typically takes from two to five years from filing, depending on the jurisdiction and the nature of the issues raised. Once a patent has been granted, it is not immune from challenge. The validity of patents can be called into question either in specific proceedings for that purpose or as part of a defence to an infringement action undertaken against a third party, depending on the jurisdiction. Any such challenge in one country will not necessarily affect the national patents within the same family in any other country.

Generally speaking, patents can last for up to 20 years, calculated from the application date (usually the PCT filing date) in each country, providing that any renewal fees necessary to maintain the patent in force are paid in due time (annually in most countries). The right to enforce a patent against a third party exists as from the date of grant; in certain jurisdictions damages can be claimed in respect of the period before the date of grant if there has been infringement of a valid claim in the application, from the date of its publication by the relevant patent office.

(b) Obtaining Patent Protection for Repurposed Drugs (new use IP)

As indicated above, the Group seeks patent protection for a new use of a known drug (known as a "second medical use patent").

If such a patent is granted then, generally, any third party offering the known drug for sale with an associated label listing the patented indication as an approved use will infringe the patent.

The Group not only seeks to gain second medical use patent protection for its product candidates, but also seeks to ensure they are differentiated from the original marketed product via a new route of delivery and dose that are appropriate for the Group's new indication. This type of product differentiation helps to ensure that the currently marketed products which contain the known drug cannot be used in a manner not approved by the healthcare regulator (known as "off label") in the indication developed and protected by the Group. In the case of the Group's product BARHEMSYS® for PONV, BARHEMSYS® was the first approval for the active ingredient amisulpride is the US by the FDA, so it is listed in the FDA's Orange Book, which provides strong protection from generics. In Europe, amisulpride has been approved as an anti-psychotic in the form of an oral tablet whereas an intravenous injection is required to manage PONV.

(c) The Group's Intellectual Property Strategy

Patent Filing Procedure used by the Group

By filing a patent application in the United Kingdom followed by an international application claiming priority therefrom, the Group seeks protection for its inventions. The Group's international applications are generally searched by the EPO in its capacity as a designated PCT International Searching Authority to identify relevant pre-existing technology. The international applications are published 18 months after the earliest priority date, following which, and if it is appropriate and beneficial to do so, the Group generally requests that international preliminary examination is conducted by the EPO.

In taking advantage of the PCT system, the Group initially designates all possible countries. Subsequently, the number of countries may be reduced to a greater or lesser extent, depending upon the Group's perception of the importance of the invention, but in most cases it pursues protection for the core IP in member countries of the EPC and in Australia, Brazil, Canada, China, Israel, Japan, Mexico, New Zealand, Republic of Korea, South Africa and the US.

(d) The Patent Portfolio

Summary of Patent Cases for BARHEMSYS® and APD403

The table below summarises, the patent portfolio (of pending patent applications and granted patents) associated with the Group's product candidates BARHEMSYS® and APD403. There have been no third party challenges to any of the Group's patents and applications to date.

Project	Application number	Earliest Priority Date	Initial term	Status
PONV	PCT/GB2011/050472	03/2010	03/2031 (02/2034 with PTE in US)	Granted in US, Australia, Mexico, New Zealand, South Korea, Israel, South Africa, Japan, China, Hong Kong, Canada, Eurasia and by the EPO. Pending in other countries where applications have been made.
PONV	PCT/GB2017/053288 PCT/GB2018/050374 ***	11/2016 02/2018 07/2020	11/2037 02/2038	Pending in all countries where applications have been made. Pending in all countries where applications have been made. Priority Application pending.
CINV	PCT/GB2011/050472	03/2010	03/2031	Granted in US, Australia, Mexico, New Zealand, South Korea, Israel, South Africa, Japan, China, Hong Kong, Canada, Eurasia and by the EPO. Pending in other countries where applications have been made.
CINV	PCT/GB2016/050998	04/2015	04/2036	Granted in Australia and US. Pending in all other countries where applications have been made.

BARHEMSYS® – PONV

This invention relates to amisulpride for the management of PONV. It was the subject of a British patent application filed in March 2010, and International patent application number PCT/GB2011/050472 filed on 10 March 2011, and published in September 2011. A patent has been granted under the EPC, with claims

directed to amisulpride for use in PONV. The patent has been granted in all available EPC-contracting states. In the US, four patents have been granted so far, with claims relating to: a method of treating PONV using a mixture containing equal amounts of enantiomers of amisulpride, at a dose of 2.5 mg to 20 mg; a method of treating PONV using amisulpride, at a dose of 1 mg to 20 mg; a method of treating PONV using amisulpride at a dose of less than 50 mg; and a pharmaceutical composition comprising amisulpride in an amount of 2.5 mg per dose or 5 mg per dose, and a pharmaceutically acceptable carrier. There is a further continuation application on file to obtain further protection for the drug. There is the option of filing further continuation applications, if desired. Patents granted on applications in this family are expected to remain in force until March 2031, subject to the payment of renewal fees. An application has been made for a patent term extension in the US, which could, if approved, extend the patent term to February 2034. A number of patient selection patent applications have been filed based on data generated in the Phase 3 clinical programme. This includes an application relating to the subset of patients where post-operative emesis would be potentially dangerous to the patent and an application relating to 'rescue' treatment of PONV, i.e. where prior prophylaxis has failed. These applications are pending, but if granted could extend protection to 2038. Upon FDA approval of amisulpride, the Group's granted patents covering BARHEMSYS® were listed in the Orange Book. The Orange Book is a database of drug products approved on the basis of safety and effectiveness by the FDA. The effect of being listed in the Orange Book is that an Abbreviated New Drug Application ("**ANDA**") (generic) applicant is required to file a certification regarding each relevant patent listed in the Orange Book, stating either that the patent has expired or that it is invalid (a "Paragraph IV filing"). A Paragraph IV filing is considered to be a technical act of patent infringement and gives the patent holder the right to initiate a patent infringement suit. If the owner of a listed patent sues for patent infringement within 45 days of receipt of notice of the Paragraph IV filing, the FDA is barred from approving the ANDA for 30 months (the 30-month stay).

APD403 – CINV

This invention was also initially the subject of a British patent application filed in March 2010, and International patent application number PCT/GB2011/050472 filed on 10 March 2011, and published in September 2011. A patent has been granted under the EPC, with claims directed to amisulpride for use in CINV. The patent has been granted in all available EPC-contracting states. In the US, there are two granted patents. The first patent that has been granted has claims directed to a method of treating CINV using amisulpride at a dose of 1 to 40 mg in combination with any other antiemetic agent. The second patent has claims directed to amisulpride (either alone or in combination) at a dose of 2.5 mg to 20 mg. Patents granted on applications in this family are expected to remain in force until March 2031, subject to the payment of renewal fees. Upon FDA approval of amisulpride, the Group's granted patents are listed in the Orange Book (see above for an explanation of the effect of being listed in the Orange Book). The Group also has a granted patent and a series of pending national applications derived from International patent application PCT/GB2016/050998 (priority date of April 2015) for a CINV kit and combination therapy for nausea and vomiting. The International Preliminary Report on patentability (issued by the EPO) indicated that there is patentable subject matter in that application. A US patent has been granted covering the combination therapy.

Amisulpride for use in OINV

Amisulpride for use in opioid-induced nausea and vomiting ("**OINV**") was also disclosed and claimed in a British patent application filed in March 2010, and International patent application number PCT/GB2011/050472 filed on 10 March 2011, and published in September 2011. A patent relating to the therapy of OINV has been granted in a number of countries including under the EPC, with claims directed to amisulpride for use in OINV. The patent has been granted in all available EPC-contracting states. In the US, one patent has been granted, with claims relating to: A method for the prevention and/or treatment of opioid-induced nausea and vomiting (OINV), comprising administering amisulpride to a subject in need thereof at a dose of less than 50 mg.

Summary of cases for BYFAVO™

There are a number of issued US patents for this product. This includes composition of matter patents, polymorph patents, dosage regimen patents and method of manufacture patents. There are also several pending applications.

As described above, with FDA approval of remimazolam, certain of the BYFAVO™ granted patents will now be listed in the Orange Book. The Orange Book is a database of drug products approved on the basis of safety and effectiveness by the FDA. The effect of being listed in the Orange Book is that an Abbreviated New Drug Application ("**ANDA**") (generic) applicant is required to file a certification regarding

each relevant patent listed in the Orange Book, stating either that the patent has expired or that it is invalid (a "Paragraph IV filing"). A Paragraph IV filing is considered to be a technical act of patent infringement and gives the patent holder the right to initiate a patent infringement suit. If the owner of a listed patent sues for patent infringement within 45 days of receipt of notice of the Paragraph IV filing, the FDA is barred from approving the ANDA for 30 months (the 30-month stay). Patent term extensions may also be available.

Summary of US Patent Cases

The table below summarises, the patent portfolio in the USA (of pending patent applications and granted patents) associated with BYFAVO™. The initial term does not include any disclaimed term, patent term adjustment, patent term extension or any other extension of term to which a patent may be entitled.

Title	Application and Grant numbers	Filing Date	Initial term	Status
Short-acting Benzodiazepines	09/980,680; 7,160,880	05/2000	05/2020	Issued
Short-acting Benzodiazepines	11/650,637; 7,435,730	05/2000	05/2020	Issued
Short-acting Benzodiazepines	11/650,635; 7,473,689	05/2000	05/2020	Issued
Short-acting Benzodiazepines	11,634,788; 7,485,635	05/2000	05/2020	Issued
Short-acting Benzodiazepines	11/650,636; 7,528,127	05/2000	05/2020	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	12/373,457; 8,642,588	07/2007	07/2027	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	12/373,472; 9,193,730	07/2007	07/2027	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	14/948,889; 9,777,007	07/2007	07/2027	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	15/703,945; 9914,738	07/2007	07/2027	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	15/908,081; 10,472,365	07/2007	07/2027	Issued
Short-acting Benzodiazepine salts and their polymorphic forms	16/598,876	10/2019	07/2027	Pending
Process for preparing 3-[(4S)-8-bromo-1-methyl-6-(2-pyridinyl)-4H-imidazo[1,2-A][1,4]benzodiazepine-4-YL]propionic acid methyl ester or the benzene sulfonate salt thereof, and compounds useful in that process	13/496,742; 9,156,842	09/2010	09/2030	Issued
Process for preparing 3-[(4S)-8-bromo-1-methyl-6-(2-pyridinyl)-4H-imidazo[1,2-A][1,4]benzodiazepine-4-YL]propionic acid methyl ester or the benzene sulfonate salt thereof, and compounds useful in that process	14/841,899, 9,512078	09/2010	09/2030	Issued
Process for preparing 3-[(4S)-8-bromo-1-methyl-6-(2-pyridinyl)-4H-imidazo[1,2-A][1,4]benzodiazepine-4-YL]propionic acid methyl ester or the benzene sulfonate salt thereof, and compounds useful in that process	15/336,143; 10,000,464	09/2010	09/2030	Issued
Compositions comprising short-acting benzodiazepines	14/402,590	05/2013	05/2033	Pending
Dosing regimen for sedation with CNS 7056 (remimazolam)	13/883,935; 9,561,236	11/2011	11/2013	Issued
Dosing regimen for sedation with CNS 7056 (remimazolam)	15,400,117; 9,737,547	11/2011	11/2031	Issued
Dosing regimen for sedation with CNS 7056 (remimazolam)	15/647,143; 9, 827,251	11/2011	11/2031	Issued
Dosing regimen for sedation with CNS 7056 (remimazolam)	15/792,636; 10,052,334	11/2011	11/2031	Issued
Dosing regimen for sedation with CNS 7056 (remimazolam)	16/039,198; 10,195,210	11/2011	11/2031	Issued
Dosing regimen for sedation with CNS 7056 (remimazolam)	16/213,879; 10,342,800	11/2011	11/2031	Issued
Dosing Regimen of Sedative	14/424,340	08/2013	08/2033	Pending
Orally inhaled and nasal benzodiazepines	16/093,112	04/2017	04/2037	Pending

(e) Summary of trade mark registrations and applications

The Group has a registered trade mark (number 3075213) (Series of 2) in the UK covering its Group logo. The Group logo is also registered as a trade mark in the European Union (EUTM) and in the US (as designations of International trade mark registration no. 1266446; the US designation has also been allocated local registration no. 4980399).

There are trade mark registrations for BARHEMSYS in the UK (no. 3292068) and in the US (no. 5620798) and a trade mark application for BARHEMSYS (no. 1913639) is pending in Canada. An international trade mark application has been filed for BARHEMSYS, which designates Switzerland, China, the European Union (EUTM), Japan, Korea, Norway and Turkey (as designations of International trade mark registration no. 1426980). Further applications for BARHEMSYS are proposed to be filed in Australia, New Zealand, South Africa, India, Israel and Brazil. A range of alternative names and spellings have also been registered as trademarks in multiple territories.

A US application has been filed for the word BYFAVO (no. 88099395-wordmark) in the name of Cosmo Technologies Limited. The trademark application was allowed in October 2019. A US application has also been filed for a BYFAVO logo (no. 88817162-stylised characters) in the name of Cosmo Technologies Limited. Pursuant to the BYFAVO™ Assignment Agreement, these trade mark applications were assigned to the Operating Company with effect from 7 August 2020.

9.3 *Data Exclusivity*

US

In the US, the Group expects its amisulpride-based products to be protected by data exclusivity (see the glossary for a brief explanation) for a period of five years from the time of FDA approval of the product candidate. Data exclusivity extends from the date of product approval, and this protection period runs concurrently with any remaining patent term protection for the product. The effect of this is that data exclusivity provides additional protection to the patentee where the remaining period of the patent is less than the period in which data exclusivity applies at the date of FDA approval or if the patent term comes to an end prior to its expiry (for example, as a result of a revocation action).

European Union

In the European Union, the first applicant for approval of a use for a medicinal product is, in effect, protected from competition by ten years of data exclusivity from the date of grant of the marketing authorisation. An additional one year may be obtained in a number of circumstances, for example where the applicant is granted a marketing authorisation for a significant new indication for the medicinal product in question. This protection period runs concurrently with the remaining life of the patent for the medicinal product. This provides additional protection to the patentee where the remaining period of the patent is less than the period in which data exclusivity applies at the date of regulatory approval or if the patent term comes to an end prior to its expiry. The Group's products may benefit from data exclusivity once the relevant marketing authorisation has been granted in the European Union.

9.4 *Supplementary Protection Certificates and Patent Term Extensions*

Upon approval of BARHEMSYS® in the US, an application for a Patent Term extension was filed. If granted, this is expected to extend the expiration of US9084765 to 26 February 2034.

Supplementary Protection Certificates ("**SPCs**") provide certain rights to the proprietor of a drug that has been patented and approved in Europe. SPCs may be filed on the basis of either a first regulatory approval in Europe of a new molecular entity or an approval of a new clinical indication for a known drug. If granted, an SPC can extend the patent protection for an approved drug beyond the standard 20 years. The duration of an SPC is equal to the time that has elapsed between the filing date of the patent and the first regulatory approval of the drug in any European country, minus five years, but the maximum duration of any SPC is five years. Therefore, upon approval of amisulpride in Europe for the new clinical indication, the Group may be granted SPCs in respect of such indications. If the drug which is the subject of an SPC application has undergone specific paediatric clinical trials, then it is possible to extend the duration of the SPC for another six months (paediatric extension).

10. **Dividend Policy**

The Company has never declared or paid any cash dividends on its Ordinary Shares. The Company intends to retain future earnings, if any, to finance the operation of its business and does not anticipate paying any

cash dividends in the foreseeable future. Any future determination related to the Company's dividend policy will be made at the discretion of the Board after considering its financial condition, results of operations, capital requirements, business prospects and other factors the Board deems relevant, and subject to the restrictions contained in any future financing instruments.

11. Insurance

The Group maintains a level of insurance which is customary for its industry to cover its activities in each territory in which it operates and usual business operations, including product liability insurance.

12. Information and Communication Technology

The Group ensures regular back-ups of its data are made and stored. The Group has introduced more comprehensive cloud-based enterprise management systems to ensure timely and secure management of its data on a worldwide basis and to enable prompt and reliable reporting of its operating and financial progress.

PART VII

DIRECTORS, SENIOR MANAGERS AND CORPORATE GOVERNANCE

1. DIRECTORS

The current members of the Board of Directors are as follows:

Name	Position	Age
Scott Byrd	Non-Executive Chairman	50
Michael (Mike) Bolinder	Chief Executive Officer	51
Edward J. Borkowski	Non-Executive Director	58
Dr John Brown	Non-Executive Director and SID	64
Alessandro Della Chà	Non-Executive Director	57

The business address of each Director is Acacia Pharma Group plc, The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH, UK.

Biographies of Directors

Scott Byrd

Scott Byrd is the independent Non-Executive Chairman of Acacia Pharma. Scott has been involved with the Group since February 2015, serving as Chief Operating Officer until 31 October 2017 when he resigned his executive role and was appointed as a Non-Executive Director. Scott now serves as president and chief executive officer and a director of Outpost Medicine which is a biopharmaceutical company focused on new treatments for urologic and gastrointestinal disorders, and chief executive officer and founder of Pioneer Therapeutics. Prior to joining Acacia Pharma, he was president and chief executive officer of SAB Strategic Advisors, LLC and has 23 years of experience in the pharmaceutical industry. He was the chief commercial officer and senior vice president of Cadence Pharmaceuticals Inc. from June 2009 until its acquisition by Mallinckrodt Pharmaceuticals plc in March 2014. Previously, Scott served in a variety of US and global roles in sales, marketing, finance, manufacturing and strategic planning at Eli Lilly and Company starting in January 1992. Scott holds a B.S. in mechanical engineering from Bradley University and an M.B.A. from Harvard Business School.

Michael (Mike) Bolinder

Mike joined Acacia Pharma in August 2015 as Vice President of Marketing and was subsequently promoted to Chief Commercial Officer in November 2017 and to Chief Executive Officer on 1 August 2019. He has more than 17 years of experience in the pharmaceutical industry. Prior to Acacia Pharma, Mike served as the Head of Marketing and Commercial Strategy for the Hospital Division at Mallinckrodt Pharmaceuticals (via the Cadence Pharmaceuticals, Inc. acquisition) which commercialised Ofirmev®, a post-operative pain control product promoted to anaesthetists and surgical teams. Prior to joining Cadence Pharmaceuticals, Inc., he worked at Eli Lilly and Company for 11 years in various sales and marketing roles of increasing responsibility across multiple therapeutic areas and successful product launches. Mike graduated from Florida State University with double majors of International Business and Spanish.

Edward (Ed) J. Borkowski

Ed is a Certified Public Accountant with significant experience in senior roles in a number of healthcare companies. He has previously served as the Executive Vice President and Chief Financial Officer of Aceto Corp., Concordia International, Amerigen Pharmaceuticals, ConvaTec Healthcare, CareFusion Corporation and Mylan and in a variety of senior finance positions at Pharmacia, American Home Products, Cyanamid and at Arthur Andersen. He is currently chairman of AzurRx BioPharma, Inc. and was a non-executive director of Codiagnostics, Inc. between June 2017 and June 2019. Most recently, he was Executive Vice President, interim Chief Financial Officer and head of strategy, legal, compliance, investor and public relations for MiMedx Group, Inc between 2018 and November 2019 and Ed is currently Executive Vice President of Therapeutics HD since January 2020. Ed holds a Bachelor of Science in Economics and Political Science from Allegheny College and a Master in Business Administration in Finance and Accounting from Rutgers University.

Dr John Brown

Dr Brown has extensive experience in the life sciences sector. He is the chairman of the Cell and Gene Therapy Catapult and a non-executive director of YourGene Health plc and BioCity Nottingham Ltd. Previously he was Chairman of Kyowa Kirin International plc, Synpromics Ltd, BTG plc, Axis-Shield plc, Touch Bionics Ltd and CXR Biosciences Ltd and a non-executive director of Quantum Pharma plc. In the public sector he is Chairman of the Roslin Foundation, a Fellow, Trustee and Treasurer of the Royal Society of Edinburgh, a Member of MRC Council and an Honorary Professor of the University of Edinburgh. He was made CBE in 2011.

Alessandro Della Chà

Alessandro has been a board member of Cosmo Pharmaceuticals N.V. since 2006 and it's Chief Executive Officer since March 2014. Previously, he was senior partner at Studio Legale Edoardo Ricci e Associati, Milan, where he specialized in company law, mergers and acquisitions. He has also worked as assistant of the central director for corporate matters at Fininvest Group and from 1994 to 1998 he was director of II.PP.A.B. Milan (formerly ECA), a charitable institution owning hospitals and specialising in elderly care. Alessandro has a degree in law from the University of Milan, Italy, and an LL.M. in European Union commercial law from the University of Leicester, UK. He is a lecturer on commercial and company law issues. Alessandro joined the Board of Acacia Pharma in April 2020.

2. SENIOR MANAGERS

In addition to the Executive Directors, Gabriel Fox is a Senior Manager serving as Chief Medical Officer. Gary Gemignani was appointed as Chief Financial Officer with effect from 1 March 2020. Both Gabriel and Gary are members of the Group's Executive Management Team.

Dr Gabriel Fox (Aged 54)

Gabriel has served in a variety of roles in clinical development, medical affairs and global marketing since joining the pharmaceutical industry in 1997. Working at NeXstar Pharmaceuticals Inc (acquired by Gilead Sciences Inc) and at F. Hoffmann-La Roche global headquarters in Basel, Switzerland, Gabriel was involved in a number of major anti-cancer drugs and cancer supportive care products, including Herceptin®, Avastin®, Tarceva®, Kytril® and AmBisome®, undertaking a wide range of tasks including clinical trial management, key opinion leader development, publication planning and worldwide marketing affiliate support. In his most recent position prior to joining Acacia Pharma in 2008, Gabriel was Head of Global Oncology Marketing at Roche. Gabriel undertook his medical training at Cambridge University.

Gary Gemignani (Aged 55)

Gary Gemignani's career in healthcare spans over three decades, including senior management/executive positions at several pharmaceutical and biopharmaceutical companies. Most recently, he served as chief financial officer of Synergy Pharmaceuticals Inc. See Section 9.3 of Part XIV (*Additional Information*).

Previously, he served as chief executive officer and chief financial officer of Biodel Inc., overseeing business and strategic planning, operations and financing activities of the company. During his tenure, Gary successfully led Biodel's reverse merger with Albireo Ltd and managed several corporate restructurings to strengthen Albireo's overall financial position. Prior to this, he served in senior and executive financial and operational roles with multiple public and private companies including, Gentium, Novartis and Wyeth. Gary started his career at Arthur Andersen & Co.

3. CORPORATE GOVERNANCE

The Directors recognise the importance of sound corporate governance. As a company incorporated in England and Wales, the shares of which are admitted to trading on the regulated market of Euronext Brussels, the Directors are aware that the Company should at least apply the corporate governance code applicable in the country of its registered office or of its listing and that it has the freedom to choose which of the two potentially applicable codes it wishes to apply if the codes are different.

Since the 2020 Belgian Code on Corporate Governance applies to Belgian companies admitted to trading on a regulated market, the Board has resolved not to apply the Belgian Code on Corporate Governance but to apply the UK Corporate Governance Code (the "**Code**") as it is deemed more appropriate, in view of the fact that the Company is incorporated in England and Wales.

The Directors support high standards of corporate governance. The Board also takes account of institutional shareholder governance rules and guidance on disclosure and shareholder authorisation of corporate events. The Board meets at least six times a year and may meet at other times as required or otherwise at the request of one or more of the Directors. The Group has applied, and complied with, the Code throughout 2020, with the exception that the constitution of the Board, Remuneration Committee and Audit Committee was not in compliance with the Code for the entire period, as explained below.

Prior to the Annual General Meeting (AGM) held on 7 April 2020, Pieter van der Meer, who was not independent, served on the Remuneration Committee, and Patrick Vink, the Non-Executive Chairman served on the Audit Committee, resulting in a breach of the Code. Both Pieter and Patrick stood down as Directors at the AGM on 7 April 2020 and, following their resignation, the constitution of the Remuneration Committee and Audit Committee is now in compliance with the Code. Furthermore, the constitution of the Board was not in compliance with the Code, as the Company did not comply with the provision that at least half the Board, excluding the chair, should be independent non-executive directors. Following the resignation of Christine Soden, an Executive Director, on 29 February 2020, and the standing down of Pieter van der Meer and Johan Kördel at the AGM on 7 April 2020, the constitution of the Board became compliant with the Code.

The Board currently comprises five members, including one Executive Director, three Non-Executive Directors and the Non-Executive Chairman. Scott Byrd, the Non-Executive Chairman, is considered to be independent for the purposes of the Code since his interests in the share capital of the Company, through vested pre-IPO options and Ordinary Shares, is not considered material. Alessandro Della Chà is not considered to be independent for the purposes of the Code as a result of his role at Cosmo, which is a significant Shareholder. The Company regards Dr John Brown and Edward J. Borkowski as independent Non-Executive Directors for the purposes of the Code.

The membership of the Committees now includes at least two independent Non-Executive Directors, and the Committees are chaired by independent Non-Executive Directors, who carry a casting vote if there is deadlock.

The Code recommends that the Board should appoint one of its independent non-executive directors to be the senior independent director (the "**SID**"). The SID should be available to Shareholders if they have concerns that the normal channels of Chairman, Chief Executive Officer or other Executive Directors have failed to resolve, or for which such channels of communication are inappropriate. Dr John Brown holds the role of SID on the Board.

4. BOARD COMMITTEES

As envisaged by the Code, the Board has established three committees: Audit, Remuneration and Nomination Committees, each with written terms of reference. If the need should arise, the Board may set up additional committees as appropriate.

4.1 *Audit Committee*

The Audit Committee has responsibility for, among other things, the monitoring of the financial integrity of the financial statements of the Group and the involvement of the Group's auditors in that process. It focuses in particular on compliance with accounting policies and ensuring that an effective system of internal financial control is maintained. The ultimate responsibility for reviewing and approving the annual report and accounts and the half-yearly reports remains with the Board. The Audit Committee normally meets at least three times a year at the appropriate times in the reporting and audit cycle.

The terms of reference of the Audit Committee cover such issues as membership and the frequency of meetings, as mentioned above, together with requirements of any quorum for and the right to attend meetings. The responsibilities of the Audit Committee covered in its terms of reference include the following: external audit, financial reporting, internal controls and risk management. The terms of reference also set out the authority of the committee to carry out its responsibilities.

The Code recommends that the Audit Committee comprises at least three members (or two, in the case of smaller companies) who are all independent non-executive directors and includes one member with recent and relevant financial experience. The Audit Committee is comprised of two members, both of whom are independent Non-Executive Directors: Edward J. Borkowski and Dr John Brown. The committee is chaired by Edward J. Borkowski who is independent and is considered to have recent and relevant financial experience.

4.2 *Remuneration Committee*

The Remuneration Committee has responsibility for determining the specific remuneration packages for each of the Executive Directors and certain senior executives of the Group, including pension rights and any compensation payments, and recommending and monitoring the level and structure of remuneration for senior management, and the implementation of share options, or other performance related schemes. It normally meets at least three times a year.

The terms of reference of the Remuneration Committee cover such issues as membership and the frequency of meetings, as mentioned above, together with requirements for quorum and the right to attend meetings. The responsibilities of the Remuneration Committee covered in its terms of reference include the following: determining and monitoring policy on and setting levels of remuneration, termination, performance-related pay, pension arrangements, reporting and disclosure, share incentive plans and remuneration consultants. The terms of reference also set out the reporting responsibilities and the authority of the committee to carry out its responsibilities.

The Code recommends that the Remuneration Committee comprises at least three members (or two, in the case of smaller companies) who are all independent non-executive directors one of whom may be the Chairman (but who may not chair the Remuneration Committee). The Remuneration Committee is comprised of three members all of whom are independent Non-Executive Directors: Dr John Brown, Edward J. Borkowski and Scott Byrd. The committee is chaired by Dr John Brown.

4.3 *Nomination Committee*

The Nomination Committee is responsible for considering and making recommendations to the Board in respect of appointments to the Board, the Board committees and the chairmanship of the Board committees. It is also responsible for keeping the structure, size and composition of the Board under regular review, and for making recommendations to the Board with regard to any changes necessary, taking into account the skills and expertise that will be needed on the Board in the future. The Nomination Committee's terms of reference deal with such things as membership, quorum and reporting responsibilities. The Nomination Committee normally meets at least twice a year.

The Code recommends that a majority of the members of the Nomination Committee should be independent non-executive directors. The Nomination Committee is comprised of three members: Scott Byrd, Dr John Brown and Alessandro Della Chà. The committee is chaired by Scott Byrd.

5. TAKEOVER REGULATION

The City Code on Takeovers and Mergers (the "**City Code**") is issued and administered by The Panel on Takeovers and Mergers (the "**Takeover Panel**"). The Company is subject to the City Code and therefore its Shareholders are entitled to certain protections afforded by the City Code. As Acacia Pharma is a company with its registered office in England and Wales that is only admitted to trading on Euronext Brussels, the shared jurisdiction rules pursuant to article 4 of the Takeover Directive apply to any takeover bid for the company. Accordingly, any takeover bid would fall under the shared jurisdiction of the UK Takeover Panel and the Belgian FSMA, who would jointly regulate the takeover bid.

The City Code would apply to the takeover bid in respect of matters relating to the information to be provided to the employees of the Company and matters relating to UK company law (in particular, the percentage of voting rights which confers control and any derogation from the obligation to launch an offer, as well as the conditions under which the Board could undertake any action which might result in the frustration of an offer) ("**employee information and company law matters**"). Such employee information and company law matters would be administered by the Takeover Panel. The Belgian Act of 1 April 2007 on takeover bids (the "**Belgian Takeover Act**") and the Belgian Royal Decree of 27 April 2007 on takeover bids (the "**Belgian Takeover Decree**" and together with the Belgian Takeover Act, the "**Belgian Takeover Laws**") would apply in relation to matters relating to the consideration offered in the context of a takeover bid (in particular the bid price per share) and matters relating to the offer procedure (in particular, the information on any bidder's decision to make a takeover bid, the contents of the relevant offer document or prospectus and the disclosure of the Takeover Bid) ("**consideration and procedural matters**"). Such consideration and procedural matters would be administered by the Belgian FSMA. The FSMA would approve the offer document or prospectus and such document or prospectus would not be subject to any other regulatory approval as the contents of such document are regulated by the Belgian Takeover Laws. Any takeover bid itself would be approved by the Belgian FSMA.

In the event that, on 31 December 2020, no legally binding agreement between the UK and the EU governing the future trade relationship has been reached, then the shared jurisdiction rules in section 3(a)(iii) of the Introduction to the City Code are likely to be deleted with effect from 11.00 p.m. on that date. As the Company is not currently considered by the Takeover Panel to have its place of central management and control in the United Kingdom, the City Code will cease to apply to any takeover bid for it with effect from this time (in the event that any takeover bid was at that time continuing) and thereafter will not apply to the Company for so long as its central management and control remains outside of the UK.

PART VIII

CAPITALISATION AND INDEBTEDNESS

You should read the following tables together with the 2018 Annual Financial Statements, the 2019 Annual Financial Statements and the 2020 Interim Financial Statements which are referred to in Part XI (*Historical Financial Information*).

The following tables set out the Group's capitalisation as at 30 June 2020 (being the date of the last published financial information of the Group) and the material changes thereto since such date and the date of this Prospectus and unaudited indebtedness and net financial indebtedness as at 30 June 2020. These statements of indebtedness and net financial indebtedness have been prepared under the IFRS accounting policies that are consistent with those used in preparing the Group's 2019 Annual Financial Statements.

The following tables: (i) have not been audited and have been sourced from the Company's internal accounting records; and (ii) do not reflect the impact of the Fundraising on the Group's capitalisation and indebtedness.

Capitalisation and indebtedness

	30 June 2020 $000's
Total current debt	
Guaranteed	—
Secured	5,296
Unguaranteed / unsecured [3]	117
Total current debt	5,413
Total non-current debt (excluding current portion of the long term debt)	
Guaranteed	—
Secured	2,488
Unguaranteed / unsecured	231
Total non-current debt	2,719
Total indebtedness	8,132
Total shareholders' equity	
Share capital	1,954
Share premium	110,083
Merger reserve	(106,625)
Share based payment reserve	5,171
Foreign currency translation reserve	(890)
Total capitalisation	9,693

Notes

1. The Group has $644 thousand of capitalised issue costs.
2. The Group's secured liabilities relate to the Hercules Capital term loan which is secured by fixed and floating charges over all of the assets of the Group.
3. The Group's unsecured liabilities relate to lease liabilities.
4. The Group has no guaranteed debt.
5. The Group has an unsecured loan facility available from Cosmo in the amount of €25 million. On 27 July 2020, the Group drew down the first tranche in the amount of €15 million in order to satisfy the €15 million cash portion of the overall €30 million milestone payment due to Cosmo on approval of BYFAVO™ by the FDA. As of the date of this Prospectus, the remaining €10 million available under the €25 million Loan Agreement is undrawn and will remain available for drawdown until 30 September 2020. Such unsecured debt will become secured debt upon the termination of the Hercules Facility. See further details in Note 16 to the 2020 Interim Financial Statements which are incorporated by reference as set out in Part XI (*Historical Financial Information*) and Section 18 (*Material Contracts*) in Part XIV (*Additional Information*) of this Prospectus. The Group intends to draw down the remaining €10 million available under the €25 million Loan Agreement on or before 30 September 2020 for the purposes of its commercialisation strategy.
6. Total Shareholders' equity does not include the profit and loss account.

7. As set out in Note 16 of the interim financial statements for the six months ended 30 June 2020, 4,923,811 shares were issued on 16 July 2020, in satisfaction of the €15 million equity portion of the overall €30 million milestone payment due to Cosmo on approval of BYFAVO™ by the FDA.
8. Pursuant to the BYFAVO™ Wind-Up Agreement, upon the first commercial sale of BYFAVO™ by the Operating Company, the Company shall, within 10 business days, issue to Cosmo such number of Ordinary Shares issued at a price per share of the volume weighted average price of the 15 trading days prior to the date of the first commercial sale of BYFAVO™ by the Operating Company as is equal to €5 million.

The following table sets out the net consolidated financial indebtedness of the Group as at 30 June 2020:

Net indebtedness

	30 June 2020 $000's
Cash	24,612
Cash equivalents	—
Cash and cash equivalents	24,612
Total liquidity	24,612
Current financial receivable	
Current bank debt[3]	5,296
Other current financial debt[4]	117
Current financial debt	5,413
Net current financial liquidity	19,199
Non-current bank loans[3]	2,488
Other non-current financial debt[4]	231
Non-current financial indebtedness	2,719
Net financial liquidity	16,480

Notes:
1. The Group has no indirect or contingent indebtedness as at 30 June 2020.
2. The Group has $644 thousand of capitalised issue costs.
3. The Group's bank debt relates to the Hercules Facility. The Group holds an additional loan facility of €25 million available from Cosmo of which €15 million has been drawn, since 30 June 2020. The remaining €10 million is available for drawdown until 30 September 2020 and the Group intends to draw down this amount for the purposes of its commercialisation strategy.
4. The Group's other financial debt relates to lease liabilities.

PART IX

SELECTED FINANCIAL INFORMATION

The selected financial information set forth below shows the Group's historical financial information and other operating information as at and for each of the years ended, 31 December 2018 and 2019 and the six months ended 30 June 2020. The statement of comprehensive income, statement of financial position and cash flow statement data set forth below has been extracted without material adjustment from, and should be read in conjunction with Part XI (Historical Financial Information). The selected financial information should also be read in conjunction with Part X (Operating and Financial Review).

With effect from 1 January 2019, the Company changed its presentational currency from pounds sterling to US dollars and the Group has presented its consolidated financial statements in US dollars since that time. Financial information presented in this Part IX (*Selected Financial Information*) and throughout this Prospectus for the financial year ended 31 December 2018 remains in pounds sterling and is derived from the audited financial statements for the year ended 31 December 2018 incorporated by reference in this Prospectus. Unaudited financial information presented in this Prospectus for the financial year ended 31 December 2018 in US dollars is derived from the unaudited comparative presented in the financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus. Financial information presented in this Prospectus for the financial year ended 31 December 2019 remains in US dollars and is derived from the audited financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus. Unless otherwise indicated, sterling amounts have been translated into US dollars using the procedures set forth below:

- Assets and liabilities were translated into US dollars at closing rates of exchange. Trading results were translated into US dollars at the rates of exchange prevailing at the dates of transaction or average rates where these are a suitable proxy. Differences resulting from the retranslation on the opening net assets and the results for the period have been taken to foreign currency translation reserve, a component within shareholders' equity.
- Share capital, share premiums and other reserves were translated at historic rates prevailing at the dates of transactions.
- All exchanges rates used were extracted from the Group's underlying financial records.

Foreign currency translation reserve was set to zero as of 1 January 2015, the transition date to IFRS. Cumulative currency translation adjustments are presented as if the Group had used US dollars as the presentation currency of its Group financial statements since that date.

The exchange rates used were as follows:

GBP / USD	FY2018	HY2018	FY2017	FY2016	FY2015	FY2014
Average rate	1.336056	1.381137	1.287513	1.350331	1.58022	—
Closing rate	1.273723	1.320829	1.349164	1.2341	1.48214	1.556723

These translations should not be considered representations that any such amounts have been, could have been or could be converted into US dollars at that or any other exchange rate as of that or any other date.

1. Consolidated statement of comprehensive income

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Continuing operations:					
Research and development expenses	(3,766)	(5,031)	(3,928)	(2,511)	(623)
Sales and marketing expenses	(6,943)	(9,336)	(14,019)	(8,103)	(7,781)
Administrative expenses	(4,326)	(5,679)	(4,447)	(2,235)	(4,373)
Operating loss	**(15,035)**	**(20,046)**	**(22,394)**	**(12,849)**	**(12,777)**
Finance income	926	1,237	432	274	39
Finance expense	(2,069)	(2,764)	(1,545)	(896)	(2,523)
Loss before income tax	**(16,178)**	**(21,573)**	**(23,507)**	**(13,471)**	**(15,261)**
Taxation credit	660	881	668	352	65
Loss for the period	**(15,518)**	**(20,692)**	**(22,839)**	**(13,119)**	**(15,196)**
Exchange differences on translation of foreign operations	1,169	(2,023)	(78)	91	360
Total comprehensive expense for the period	**(14,349)**	**(22,715)**	**(22,917)**	**(13,028)**	**(14,836)**
Basic and diluted losses per Ordinary Share	(35)p	$(0.47)	$(0.43)	$(0.25)	$(0.24)

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

2. Consolidated statement of financial position

	31 December 2018 £'000 audited	31 December 2018 $'000 unaudited[1]	31 December 2019 $'000 audited	30 June 2020 $'000 Unaudited
Assets				
Non-Current Assets				
Right-of-use asset	—	—	**372**	**325**
Intangibles	—	—	—	11,180
Total Non-Current Assets	—	—	**372**	**11,505**
Other receivables	312	397	609	221
Current income tax assets	686	874	679	700
Cash and cash equivalents	29,353	37,443	17,009	24,612
Total Current Assets	**30,351**	**38,714**	**18,297**	**25,533**
Total Assets	**30,351**	**38,714**	**18,669**	**37,038**
Equity and Liabilities				
Equity attributable to equity holders				
Share capital	1,067	1,581	1,619	1,954
Share premium	54,858	75,454	75,588	110,083
Profit and loss account	31,357	54,078	31,225	16,029
Share-based payments reserve	997	1,354	3,791	5,171
Merger reserve	(69,136)	(106,625)	(106,625)	(106,625)
Foreign currency translation reserve	—	(1,172)	(1,250)	(890)
Total Equity	**19,323**	**24,670**	**4,348**	**25,722**
Liabilities				
Non-current liabilities				
Loans and other borrowings	6,968	8,867	4,701	2,719
	6,968	**8,867**	**4,701**	**2,719**
Current liabilities				
Trade and other payables	3,726	4,727	4,167	3,184
Loans and other borrowings	334	450	5,453	5,413
	4,060	**5,177**	**9,620**	**8,597**
Total Liabilities	**11,028**	**14,044**	**14,321**	**11,316**
Total Equity and Liabilities	**30,351**	**38,714**	**18,669**	**37,038**

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented as of 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

3. Consolidated cash flow statement

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Cash flows from operating activities:					
Cash used in operations	(11,972)	(15,863)	(20,665)	(14,453)	(11,942)
Income tax credit received	323	432	834		
				—	
Net cash used in operating activities	**(11,649)**	**(15,431)**	**(19,831)**	**(14,453)**	**(11,942)**
Cash flows from investing activities:					
Interest received	**202**	**246**	**432**	**271**	**39**
Net cash generated from investing activities	**202**	**246**	**432**	**271**	**39**
Cash flows from financing activities:					
Proceeds of issuance of Ordinary Shares	—	49,379	180	—	22,339
Issue costs of Ordinary Shares	35,832	(2,296)	(8)	—	(255)
Repayments of lease liabilities – principal and interest	(1,652)	—	(101)	(56)	(58)
Loan proceeds	7,671	10,000	—	—	
Costs of securing term loan	(494)	(644)	—	—	
Loan repayments	(4,500)	(6,215)	—	—	(2,221)
Interest and fees paid on loans	(1,193)	(1,324)	(998)	(504)	(427)
Net cash (used in) / generated from financing activities	**35,664**	**48,900**	**(927)**	**(506)**	**19,378**
Net (decrease) / increase in cash and cash equivalents	24,217	33,715	(20,326)	(14,742)	7,475
Cash and cash equivalents at beginning of the period	3,070	4,142	37,443	(37,443)	17,009
Effect of exchange rate movements on cash held	2,066	(414)	(108)	28	128
Cash and cash equivalents at end of the period	**29,353**	**37,443**	**17,009**	**22,729**	**24,612**

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

PART X

OPERATING AND FINANCIAL REVIEW

The following review of the Group's financial condition and operating results should be read in conjunction with the historical financial information set out in Part XI (Historical Financial Information), and with the information relating to the business of the Group included elsewhere in this document, including Part VI (Information on the Company and the Group).

The Company's published interim report and unaudited financial statements for the six months ended 30 June 2020, annual report and audited financial statements of the Company for the year ended 31 December 2019 and annual report and audited financial statements of the Company for the year ended 31 December 2018 are available on the Company's website using the following hyperlinks:

(a) interim report and unaudited consolidated financial statements for the six months ended 30 June 2020: https://www.acaciapharma.com/files/download/179;

(b) annual report and audited consolidated financial statements for the year ended 31 December 2019: https://www.acaciapharma.com/files/download/172; and

(c) annual report and audited consolidated financial statements for the year ended 31 December 2018: https://www.acaciapharma.com/files/download/158.

No part of these documents is incorporated by reference in this document, except as set out in Part XI (Historical Financial Information). The non-incorporated parts of the interim report and financial statements and annual report and financial statements are either not relevant to investors or are covered elsewhere in this document.

In addition to historical information, the following review and other parts of this Prospectus contain forward-looking statements based on the Directors' current expectations and assumptions about the Group's future business. These forward-looking statements involve risks and uncertainties. The Group's actual results could differ materially from those contained in the forward-looking statements as a result of a number of factors including, but not limited to, the risk factors set out in Part II (Risk Factors) and the factors stated in the paragraph entitled "Forward-looking statements" in Part V (Presentation of Information). Prospective investors should read the whole of this document. The results of operations for the periods reflected herein are not necessarily indicative of results that may be expected for future periods.

The following discussion focuses on the historical financial information of the Group for the two years ended 31 December 2019 prepared in accordance with IFRS as adopted by the European Union and on the basis of preparation as described in Note 1 (Summary of significant accounting policies-Basis of Preparation) to the 2019 Annual Financial Statements.

1. Overview

Acacia Pharma is a commercial stage biopharmaceutical company focused on developing and commercialising novel products to improve the care of patients undergoing serious medical treatments such as surgery, invasive procedures, or chemotherapy.

The Group's portfolio includes two FDA-approved products: BARHEMSYS®, a dopamine antagonist which has been developed for the prevention and treatment of post-operative nausea and vomiting (PONV), and BYFAVO™, a rapid onset/offset intravenous benzodiazepine sedative for use during certain invasive medical procedures in adult patients. In addition, the Group is developing an additional antiemetic product candidate, APD403, for chemotherapy-induced nausea and vomiting (CINV). The Group plans to launch both BARHEMSYS® and BYFAVO™ commercially in the US in the second half of 2020.

The Group was founded in 2007 and is based in Cambridge, UK with US operations based in Indianapolis, Indiana. The Group has financed its operations and development activities to-date through a combination of support from strategic and specialist investors, partnerships and other debt and equity financing, including through its initial public offering on Euronext Brussels in in March 2018. Specifically, the Group has raised £43.0 million of private shareholder equity, primarily from Lundbeckfond, Novo, F-Prime and Gilde, and €38.1 million from the proceeds of its IPO (net of expenses). In June 2018, the Group secured and drew down $10 million pursuant to a term loan facility with Hercules Capital. This year, in connection with the BYFAVO™ Acquisition, the Group has secured new equity investments from Cosmo totalling €20 million, together with up to €25 million in debt financing that became available on the FDA approval of BYFAVO™, of which €15 million has been drawn down and €10 million is available for drawdown until

30 September 2020. Since its inception, the Group has also benefited from the receipt of £9.8 million in R&D tax credits.

2. Recent Developments

2.1 COVID-19

The Group's business has been affected by the recent COVID-19 pandemic. Depending on the further development of the pandemic, its effect on US hospitals and the healthcare system, rules or restrictions with regard to social distancing and other containment measures, and effects on the economy and the healthcare sector in particular, the COVID-19 pandemic may continue to materially affect the Group's operations and business plan, particularly the Group's commercialisation plans. The Group may not have access to hospitals and other healthcare settings as anticipated, and may need to undertake alternative commercialisation strategies through virtual engagement and/or may need to adjust or delay the hiring of sales and related personnel, among other things. Please see Part II (*Risk Factors*) under the heading "*Risks Relating to the Group's Business Activity and Industry*" for a discussion of how COVID-19 has, and may continue to affect the Group's business.

2.2 BYFAVO Approval and Related Matters

The FDA approved the NDA for BYFAVO™ on 2 July 2020 and the Group intends to proceed with commercialisation of BYFAVO™ alongside BARHEMSYS® in the second half of 2020. The approval of BYFAVO™ has triggered certain rights and obligations under our financing and licensing agreements with Cosmo. Upon approval of BYFAVO™ by the FDA, consideration was due under the BYFAVO™ Wind-Up Agreement (which terminated the BYFAVO™ Sub-Licensing Agreement, but retained certain rights and obligations thereunder, including such consideration) in the amount of €30 million, which was satisfied in part by the issue of 4,923,811 Ordinary Shares issued at €3.046 per Ordinary Share on 16 July 2020, with the remaining amount satisfied in cash in the amount of €15 million. The Group drew down €15 million of the monies available under the €25 million Loan Agreement on 27 July 2020 in order to finance such milestone payment. The remaining €10 million is available for draw-down until 30 September 2020 and the Group expects to draw down this amount for the purposes of its commercialisation strategy.

With effect from 7 August 2020, the Group's licensing of BYFAVO™ was altered such that Cosmo assigned to the Group its US licence for BYFAVO™. From that date, the Group licenses BYFAVO™ directly from Paion, but the remaining terms of the BYFAVO™ Sub-Licensing Agreement that the Group entered into with Cosmo in January 2020 apply under the BYFAVO™ Wind-Up Agreement and remain materially unchanged. Cosmo is no longer a party to the BYFAVO™ Head-Licence Agreement.

3. Factors Affecting Comparability of Periods Under Review

With effect from 1 January 2019, the Company changed its presentational currency from pounds sterling to US dollars and the Group has presented its consolidated financial statements in US dollars since that time. Financial information presented in this section for the financial year ended 31 December 2018 remains in pounds sterling and is derived from the audited financial statements for the year ended 31 December 2018 incorporated by reference in this Prospectus, limiting comparison with other periods. Unaudited financial information presented in this Prospectus for the financial year ended 31 December 2018 in US dollars is derived from the unaudited comparative presented in the financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus. Financial information presented in this Prospectus for the financial year ended 31 December 2019 remains in US dollars and is derived from the audited financial statements for the year ended 31 December 2019 incorporated by reference in this Prospectus. Unless otherwise indicated, sterling amounts have been translated into US dollars using the procedures set forth below:

- Assets and liabilities were translated into US dollars at closing rates of exchange. Trading results were translated into US dollars at the rates of exchange prevailing at the dates of transaction or average rates where these are a suitable proxy. Differences resulting from the retranslation on the opening net assets and the results for the period have been taken to foreign currency translation reserve, a component within shareholders' equity.
- Share capital, share premiums and other reserves were translated at historic rates prevailing at the dates of transactions.
- All exchanges rates used were extracted from the Group's underlying financial records.

Foreign currency translation reserve was set to zero as of 1 January 2015, the transition date to IFRS. Cumulative currency translation adjustments are presented as if the Group had used US dollars as the presentation currency of its Group financial statements since that date.

The exchange rates used were as follows:

GBP / USD	FY2018	HY2018	FY2017	FY2016	FY2015	FY2014
Average rate	1.336056	1.381137	1.287513	1.350331	1.58022	—
Closing rate	1.273723	1.320829	1.349164	1.2341	1.48214	1.556723

These translations should not be considered representations that any such amounts have been, could have been or could be converted into US dollars at that or any other exchange rate as of that or any other date. See "*Exchange Rate Information*" elsewhere in this prospectus.

As a result of the BYFAVO™ Acquisition, an intangible asset of $11.20 million is shown in the consolidated statement of financial position as at 30 June 2020 which was not represented in prior periods. The cash position of the Company has also increased from $17.009 million as at 31 December 2019 to $24.612 million as at 30 June 2020, as well as an increase in the total equity of the Company from $4.348 million as at 31 December 2019 to $25.7 million as at 30 June 2020.

4. Factors Affecting Results of Operations

4.1 Availability of funds and capital; financing arrangements

As the Group transitions toward the commercial stage the Directors expect the Group to continue to incur losses for the foreseeable future, and expect these losses to increase following the launches of BARHEMSYS® and BYFAVO™.

The Directors anticipate significant costs to allow the Group to complete the establishment of its sales and marketing infrastructure, to launch BARHEMSYS® and BYFAVO™ to the hospital market in the US in late-2020 and to promote the products. Such costs include recruitment of a salesforce and the successful commercialisation of BARHEMSYS® and BYFAVO™.

In its pre-commercialisation stage, research and development was central to the Group's business and it continues to remain significant. The Group's research and development expenses have reduced since 2016, when there was significant expenditure on Phase 3 studies for BARHEMSYS®, with costs reducing upon completion of those studies and into 2019. The Group expects research and development expenses to increase again in the future to complete further Phase 2 and Phase 3 studies for APD403.

Because of the numerous risks and uncertainties associated with product development, the Group is unable to determine with certainty the duration and completion costs of the future clinical studies of its product candidates. The Group will determine which programmes to pursue and how much to fund each programme in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate's commercial potential.

The net proceeds of the Fundraising, together with the Group's existing cash resources and loan facilities, are expected to allow the Group to complete the establishment of its sales and marketing infrastructure, to launch BARHEMSYS® and BYFAVO™ to the hospital market in the US in late-2020 and to promote the products until the fourth quarter of 2021.

The Group's future funding requirements will depend on many factors, including, but not limited to:

- the amount of sales and other revenues the Group can generate, including the sales price and availability of adequate third-party reimbursement;
- the cost of establishing and maintaining sales, marketing and distribution capabilities for BARHEMSYS®, BYFAVO™ or any other product candidate for which the Group may receive regulatory approval;
- the cost and timing of obtaining commercial-scale product supply;
- the outcome, timing and cost of regulatory approvals, the potential for the FDA or comparable regulatory authorities to require that more or different studies need to be performed than currently expected or that the application approval is not granted for each individual indication sought. In

addition, any resubmission, amendment or failed applications to the FDA will incur additional costs and will result in delays in securing marketing approval and the availability of the Group's drugs to patients;

- the effect of competing technological and market developments and the time and cost to respond to them;
- the initiation, progress, timing, costs and results of clinical trials for the Group's product candidates, including the ability to enrol patients in a timely manner; and
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

The Group has financed its development activities by raising £43.0 million of private shareholder equity, primarily from Lundbeckfond, Novo, F-Prime and Gilde, and €38.1 million from the proceeds of its IPO (net of expenses). In June 2018, the Group secured and drew down $10 million pursuant to a term loan facility with Hercules Capital. This year, in connection with the BYFAVO™ Acquisition, the Group has secured new equity investments from Cosmo totalling €20 million, together with up to €25 million in debt financing that became available on the FDA approval of BYFAVO™, of which €15 million has been drawn down and €10 million is available for drawdown until 30 September 2020. Since its inception, the Group has also benefited from the receipt of £9.8 million in R&D tax credits.

The Group will be required to seek additional funds to finance future requirements through debt or equity offerings. Additional capital may not be available on acceptable terms, or at all. A lack of available financing for future requirements could affect the Group's costs, future expansion or sales. In addition, offering of further debt could result in additional finance expenses.

4.2 Sales of BARHEMSYS® and BYFAVO™

(a) Pricing, market access and acceptance

The revenue that the Group may generate from the sale of any products approved for sale will be primarily determined by the volume of products sold as well as the price the Group is able to achieve for such products. The commercial success of BARHEMSYS®, BYFAVO™ and any of the Group's other future products will depend on the rate and degree of market acceptance of these products among physicians, patients, healthcare payors and the medical community. The commercial success of BARHEMSYS®, BYFAVO™ and any of the Group's future products will depend upon the acceptance of such products as safe and effective by the medical community and patients and the products' pharmacoeconomic benefits. In particular, BARHEMSYS® and BYFAVO™ will not be generally be available for use by surgical teams until they have been accepted by their hospital's P&T committee and included on the formulary of approved products within that hospital. The rate and speed of acceptance will directly impact on the commercial success of the product. The market acceptance of the Group's products could be affected by a number of other factors, including:

- the safety and efficacy of the products, as well as the acceptance by physicians and patients of the products as safe and effective;
- the cost-effectiveness and availability of coverage on formularies and adequate reimbursement for the products;
- the availability and terms of contracts with group purchasing organisations;
- the success of existing products addressing the Group's target markets or the emergence of equivalent or superior products;
- changes in the standard of care for the targeted indications for any product candidate;
- sales, marketing and distribution support;
- potential product liability claims;
- relative convenience, ease of administration and other perceived advantages over alternative products and therapies;
- the resources and the effectiveness of potential partners;
- prevalence and severity of adverse events or publicity;

- limitations, precautions, warnings and other wording in the summary of product characteristics, patient information leaflet, package labelling or instructions for use;
- our ability to enter into any licensing and/or distribution agreements for BARHEMSYS® and APD403 outside the United States or receive payments thereunder (e.g., royalty payments for licensed products) and receipt of any necessary approvals and consents relating thereto; and
- any disputes with prospective partners or future partners with whom we enter into a licensing and/or distribution agreement, including disagreements over proprietary rights or contract interpretation that might disrupt our commercialisation outside the United States or lead prospective partners to develop a competing product.

Hospitals and third party payors are increasingly exerting pressure on pricing and reviewing the cost-effectiveness of medical products, therapies and services, and the downward pressure on healthcare costs has become intense in many jurisdictions. In the US, hospitals are financially incentivised to improve the quality of care and consequent patient satisfaction, as well as patient throughput. Appropriate management of PONV is a key to improving patient satisfaction scores which directly impact the reimbursement a hospital receives under Medicare within current healthcare legislation, as well as reducing post-surgical patient recovery times.

(b) Licensing agreements

The commercial plans of the Group include generating revenue from a combination of direct product sales (expected to be principally in the US) and, in the future, licence fees, milestone payments and royalties resulting from establishing licensing and/or distribution arrangements in respect of BARHEMSYS® and any future products with partners in selected non-US territories. The Group does not currently have any such licensing or distribution arrangements in place. The Group expects that any revenues it may generate will fluctuate from year to year as a result of the amount and timing of payments that the Group receives upon the sale of its products and the timing and value of any partnership deals it enters into, to the extent that any products are approved outside the US and are successfully commercialised.

The Group's sales of BYFAVO™ rely on the BYFAVO™ Assignment Agreement entered into with Paion and Cosmo, and the BYFAVO™ Wind-Up Agreement entered into with Cosmo, pursuant to which the Group has the right to develop, commercialise and manufacture BYFAVO™ in the US. The BYFAVO™ Assignment Agreement became effective on 7 August 2020. Under this agreement, the Group will be required to pay royalties on net sales of BYFAVO™ to Paion of (i) 20 per cent of net sales per calendar year up to a total amount of net sales of US$200 million; (ii) 25 per cent of net sales per calendar year for net sales exceeding US$200 million (on the amount exceeding US$200 million); and (iii) 10 per cent of net sales per calendar year after the expiration of the last-to expire licensed patent and as long as the Operating Company enjoys market exclusivity. Such royalties will reduce revenues from the sale of BYFAVO™ once these thresholds are met. Milestones shall also be payable to Paion by the Operating Company of (i) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a second indication; and (ii) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a third indication.

The Group has been and will be required to pay certain additional milestone payments to Cosmo pursuant to the BYFAVO™ Sub-Licence Agreement and the BYFAVO™ Wind-Up Agreement: (i) payment of €10 million, which was satisfied by the issue of new Ordinary Shares; (ii) payment of €30 million upon approval of BYFAVO™ by the FDA, which was settled in full as follows: (a) by the issue of 4,923,811 Ordinary Shares issued at €3.046 per Ordinary Share on 16 July 2020, plus (b) €15 million in cash, which was paid on 27 July 2020; (iii) payment of €5 million upon the first commercial sale of BYFAVO™ by the Operating Company, which is expected be satisfied by the issue of New Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the date of the the first commercial sale of BYFAVO™ by the Operating Company; (iv) US$5 million in cash upon the Operating Company first achieving US$50 million in annual "net sales" (being gross sales less returns, customary discounts and chargebacks); (v) US$10 million in cash upon the Operating Company first achieving US$100 million in annual net sales; (vi) US$15 million in cash upon the Operating Company first achieving US$150 million in annual net sales; (vii) US$20 million in cash upon the Operating Company first achieving US$200 million in annual net sales; (viii) US$25 million in cash upon the Operating Company first achieving US$250 million in annual net sales; and (ix) US$30 million in cash upon the Operating Company first achieving US$300 million in annual net sales.

4.3 Establishment of a sales and marketing infrastructure

The Group plans to add approximately 30 sales staff and 10 support staff to complete the sales and marketing organisation comprised of experienced sales, marketing, operations, regulatory and medical affairs employees targeted at the launch of BARHEMSYS® and BYFAVO™. The Group plans to increase the sales force to approximately 60 representatives within 36 months of launch if demand for the product grows. Recruiting and retaining such employees will be a significant factor affecting the success of our sales strategy and the establishment of such a commercial team is expected to impose significant costs, and losses in the short term before any revenues can be realised from the commercialisation of BARHEMSYS® and BYFAVO™.

Because a substantial portion of the prescribing activity arises in a relatively limited number of institutions, the Directors believe that the Group can successfully promote its products with such a sales force by focusing on those institutions that account for a substantial proportion of the hospital surgical market. The sales force is critical to promoting the acceptance of BARHEMSYS® and BYFAVO™ onto hospital formularies by persuading P&T committees of the clinical and pharmacoeconomic benefits of the product. The Group expects that this sales and marketing infrastructure could also be applied to commercialise APD403 (for CINV) to oncologists with a moderate increase in size.

4.4 Effects of the spread of COVID-19

The spread of COVID-19 has raised concerns that the Group or its suppliers may be impacted by the pandemic or the measures being taken to combat it. Quarantines, restrictions on travel, restrictions on public gatherings, and government measures to close business deemed to be non-essential have threatened to restrict the Group's supply chain and commercialisation efforts. For instance, the initial spread of COVID-19 in Italy raised concerns that the manufacture of certain products might be impacted. The spread of the virus in the US has impacted the US market, where the Group intends to focus its efforts to commercialise BARHEMSYS® and BYFAVO™. For instance, it has restricted and continues to restrict the Group's ability to engage in conferences and in-person access to hospitals and their Pharmacy & Therapeutics ("P&T") committees. The Group has thus far shifted its efforts to remote and virtual outreach. In addition, the majority of hospitals have postponed or cancelled all unnecessary and elective surgeries. Surgical postponements and cancellations, reduce the need for the Group's products and may impact our ability to commercialise BARHEMSYS® and BYFAVO™.

Whilst the situation has created certain challenges in accessing decision makers in hospitals and ambiguity around the timing for the resumption of their formulary committee meetings, the COVID-19 situation has created opportunities for the Group as it has led to drug shortages for the most commonly used procedural sedatives like midazolam and propofol as well as antiemetics like ondansetron and dexamethasone, all of which are currently on the FDA drug shortages list. It has also created potential procedural backlogs and pent up demand for the launch of the Group's products as hospitals and surgical centers now need to significantly increase their patient throughput, which has heightened the value proposition for both drugs in order to regain lost profits.

The extent to which COVID-19 could impact the Group's business depends on future developments, which are highly uncertain, cannot be predicted and are outside of its control, including new information which may quickly emerge concerning the severity of the virus, the scope of the pandemic and actions to contain the virus or treat its impact. The Group's business may be adversely affected by the recent outbreak if it continues to impact the conduct of surgical procedures or disrupts supply chains critical to supply of its products. If access to P&T committees is limited the Group may delay its plans to recruit a sales force as currently planned. Please see Part II (*Risk Factors*) under the heading "*Risks Relating to the Group's Business Activity and Industry*" for further discussion of how COVID-19 has, and may continue, to restrict our access to healthcare settings and postpone medical conferences and surgeries, with implications for the Group's strategic plan and business prospects.

5. Principal Components of Results of Operations

5.1 Revenue, distribution and cost of goods

The Group currently has two products approved for sale, BARHEMSYS® and BYFAVO™, in the US, which have not yet been launched nor generated any revenue. The Group does not expect to generate revenue from product sales before at least the second half of 2020, with launch of each planned for the second half of 2020. Additionally, the Group expects that revenue from product sales will be modest in the initial period following launch, while hospital formulary access is obtained before increasing gradually over time if the product gains market access and acceptance.

As the Group's commercialisation plans are focused principally on the US, the Group expects that the majority of its revenue and commercialisation costs will be denominated in US dollars. Future manufacturing costs are estimated by the Directors to be less than 10 per cent of the proposed sales price in the case of BARHEMSYS® and, for BYFAVO™, the gross margins are expected to be typical of margins across the pharmaceutical industry.

5.2 Research and development expenses

The Group previously devoted substantially all of its resources to research and development efforts relating to its product candidates, including carrying out pre-clinical research and development, conducting clinical studies, providing general and administrative support for these operations and protecting the Group's intellectual property. The Group recognises research and development expenses in its statement of comprehensive income as they are incurred.

The Group's research and development expenses consist primarily of:

- clinical research and development activities, which include fees incurred under agreements with CROs, investigative sites and consultants to carry out the clinical studies;
- research and development activities relating to formulation development and pre-clinical development activities, which include fees incurred under agreements with CROs, investigative sites and consultants that conduct a substantial portion of the non-clinical studies; and
- other costs associated with non-clinical activities, regulatory approvals (such as filing fees for the FDA and other regulatory bodies) and business development.

5.3 Sales and marketing expenses

The Group has incurred significantly higher sales and marketing expenses as it transitions into its commercialisation stage. Such expenses are associated with promotional activities for BARHEMSYS® and BYFAVO™ and building a sales and marketing team. The Group expects to increase its employee base significantly as it moves to the commercialisation of BARHEMSYS® and BYFAVO™. The Group has expanded its employee base from six employees as at the time of its IPO in 2018 to 37 full-time employees as at the date of this Prospectus and is expected to increase its employee base to approximately 80 following the full launch of BARHEMSYS® and BYFAVO™. If BARHEMSYS® and BYFAVO™ are successful, the Group expects to expand its sales and marketing infrastructure and, assuming APD403 receives marketing authorisation, to further support the launch of APD403. The Group anticipates that the expected increase in the employee base will result in a significant increase in personnel expenses in the near to medium term. Furthermore, the Group expects to incur significant additional costs in commercialising BARHEMSYS® and BYFAVO™, including the costs of market research, scientific and medical meetings, KOL education and support. The Directors anticipate the total incremental cost for the ramp up of the commercialisation plan, including hiring the approximately 30 sales staff and 10 support staff to complete the sales and marketing organisation, will be approximately $9 million per annum.

5.4 Administrative expenses

Administrative expenses consist principally of salaries and related costs for personnel in executive, finance and business development functions. Other administrative expenses include rent, travel and entertainment, patent filing and maintenance costs, costs relating to the defence and enforcement of the Group's IP and professional fees for legal, consulting, auditing and tax services. General and administrative expenses include costs relating to raising capital, such as the costs incurred in 2018 in conducting the IPO and listing on Euronext Brussels. General and administrative expenses will increase in periods with increased professional fees (including fees of accountants, lawyers and other advisers) associated with fundraising.

5.5 Finance income and expense

Finance income consists of interest income earned on the Group's cash and cash equivalents as well as its short-term investments. Finance expense has consisted of charges under the term loan facilities completed in February 2016 and June 2018, finance charges on the Company's A ordinary shares, B preferred shares and C preferred shares relating to the deemed dividend and interest accruing on such shares, in each case at 8 per cent per annum, with accumulated dividends capped at 50 per cent of the original amount subscribed for the shares. In November 2017, the Company issued £3.4 million of convertible loan notes bearing interest at 8 per cent.

All of the outstanding S ordinary shares, A ordinary shares, B preferred shares and C preferred shares automatically converted into Ordinary Shares on a 1-for-1 basis on 5 March 2018, and the accrued

dividends on such shares were settled through a pro-rata allocation of additional Ordinary Shares rather than a cash payment. The D preferred shares and the convertible loan notes and any accrued interest thereon also automatically converted into Ordinary Shares on a 1.5-for-1 basis on 5 March 2018.

Finance income and expense also reflects gains and losses due to foreign exchange that relate to borrowings and cash and cash equivalents. All other foreign exchange gains and losses are presented in the income statement within administrative expenses.

5.6 Taxation

The Group is loss making and therefore has not paid any corporation tax. The Group is entitled to claim tax credits in the United Kingdom for certain qualifying research and development expenditure. The level of such tax credits is dependent on the size of the company, as determined in accordance with criteria established by HMRC. During the period under review, the Group qualified for the "small or medium-sized enterprise" scheme (currently available for companies with less than 500 employees and either (i) an annual turnover not exceeding €100 million or (ii) gross assets not exceeding €86 million). The amount included in the Group's statement of comprehensive income as taxation represents the research and development tax credits receivable by the Group for the year, which the Group receives in cash usually three to four months after the relevant year end. Certain additional research and development and other expenditure (beyond that entitling the Group to claim tax credits) has generated tax losses which may be available to the Group to the extent that it has an obligation to pay corporation tax in the future.

6. Results of Operations

The historical financial information for the year ended 31 December 2019 has been extracted from the financial statements for the year ended 31 December 2019. The historical financial information in US dollars for the year ended 31 December 2018 has been extracted from the unaudited comparative of the financial statements for the year ended 31 December 2019. The historical financial information in pounds sterling for the year ended 31 December 2018 has been extracted from the financial statements for the year ended 31 December 2018. The financial statements for the two years ended 31 December 2019 and the interim financial statements for the six months ended 30 June 2020 are set out in this Prospectus in Part XI (*Historical Financial Information*).

The tables below sets forth certain key line items from the Group's statement of comprehensive income for the periods indicated:

Consolidated Statement of Comprehensive Income

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Continuing operations:					
Research and development expenses	(3,766)	(5,031)	(3,928)	(2,511)	(623)
Sales and marketing expenses	(6,943)	(9,336)	(14,019)	(8,103)	(7,781)
Administrative expenses	(4,326)	(5,679)	(4,447)	(2,235)	(4,373)
Operating loss	**(15,035)**	**(20,046)**	**(22,394)**	**(12,849)**	**(12,777)**
Finance income	926	1,237	432	274	39
Finance expense	(2,069)	(2,764)	(1,545)	(896)	(2,523)
Loss before income tax	**(16,178)**	**(21,573)**	**(23,507)**	**(13,471)**	**(15,261)**
Taxation credit	660	881	668	352	65
Loss for the period	**(15,518)**	**(20,692)**	**(22,839)**	**(13,119)**	**(15,196)**
Exchange differences on translation of foreign operations	1,169	(2,023)	(78)	91	360
Total comprehensive expense for the period	**(14,349)**	**(22,715)**	**(22,917)**	**(13,028)**	**(14,836)**
Basic and diluted losses per Ordinary Share	(35)p	$(0.47)	$(0.43)	$(0.25)	$(0.24)

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

6.1 Research and development expenses

Research and development costs decreased by $1.9 million, or 76 per cent, from $2.5 million in the six months ended 30 June 2019 to $0.6 million in the six months ended 30 June 2020. This decrease was due primarily to the shift towards a commercial-stage company, with limited research and development expenditure required in 2020.

Research and development costs decreased by $1.1 million, or 21.9 per cent, from $5.0 million in the year ended 31 December 2018 to $3.9 million in the year ended 31 December 2019. This decrease was due primarily to a reduction in activities surrounding product development in 2019 and efforts to curtail costs following the receipt of the CRL in May 2019.

6.2 Sales and marketing expenses

Sales and marketing expenses decreased by $0.3 million, or 4 per cent, from $8.1 million in the six months ended 30 June 2019 to $7.8 million in the six months ended 30 June 2020. This decrease was due primarily to the decrease in activity, particularly travel and conference costs, occurring as a result of COVID-19.

Sales and marketing expenses increased by $4.7 million, or 50.2 per cent, from $9.3 million in the year ended 31 December 2018 to $14.0 million in the year ended 31 December 2019, driven by the costs of recruiting and running our new commercial team and significant pre-launch marketing, education, training, distribution, regulatory and other activities relating to BARHEMSYS®.

6.3 Administrative expenses

General and administrative expenses increased by $2.2 million, or 96 per cent, from $2.2 million in the six months ended 30 June 2019 to $4.4 million in the six months ended 30 June 2020. This increase was due primarily to legal and other costs associated with the BYFAVO™ Acquisition, together with increased staffing costs.

General and administrative expenses decreased by $1.2 million, or 21.7 per cent, from $5.7 million in the year ended 31 December 2018 to $4.4 million in the year ended 31 December 2019. This decrease was due primarily to extraordinary professional costs relating to the IPO and listing on Euronext Brussels that were incurred in 2018.

6.4 Finance Income

Finance income decreased by $0.2 million, or 86 per cent, from $0.3 million in the six months ended 30 June 2019 to $0.1 million in the six months ended 30 June 2020. This reduction was due primarily to a reduction on interest income on short-term deposits as a result of lower cash balances and the historically low interest rates.

Finance income decreased by $0.8 million, or 65.1 per cent, from $1.2 million in the year ended 31 December 2018 to $0.4 million in the year ended 31 December 2019. This decrease was due primarily to the lower cash balances held and a foreign exchange loss of $0.1 million in the year ended 31 December 2019 compared to a gain of $0.9 million in in the year ended 31 December 2018.

6.5 Finance expense

Finance expense increased by $1.6 million, or 182 per cent, from $0.9 million in the six months ended 30 June 2019 to $2.5 million in the six months ended 30 June 2020. This increase was due primarily to an increase in foreign exchange losses of $0.9 million and the break fee paid on conversion of a loan facility to a cash investment ($0.8 million), offset by decreased interest costs on the Hercules Facility of $0.1 million.

Finance expense decreased by $1.2 million, or 44.1 per cent, from $2.8 million in the year ended 31 December 2018 to $1.5 million in the year ended 31 December 2019. This decrease was due primarily to decreased interest expenses after preferred shares and convertible loan notes were converted into ordinary shares in connection with the IPO, partially offset by increased loan interest and foreign exchange losses in 2019.

6.6 Taxation

Tax credits decreased by $0.3 million, or 82 per cent, from $0.4 million in the six months ended 30 June 2019 to $0.1 million in the six months ended 30 June 2020. This decrease was due primarily to the reduction in research and development activity in 2020.

Tax credits decreased by $0.2 million, or 24.2 per cent, from $0.9 million in the year ended 31 December 2018 to $0.7 million in the year ended 31 December 2019. This decrease was due to the decrease in qualifying research and development expenditure incurred as the result of a reduction in activities surrounding product development in 2019.

6.7 Loss for the period

As a result of the above factors:

- the loss increased by $2.0 million, or 16 per cent, from $13.1 million for the six months ended 30 June 2019 to $15.2 million for the six months ended 30 June 2020; and
- the loss increased by $2.1 million, or 10.4 per cent, from $20.7 million for the year ended 31 December 2018 to $22.8 million for the year ended 31 December 2019.

7. Liquidity and Capital Resources

7.1 Sources and uses of funds

The Group has incurred losses since inception and resulting negative cash flows from operating activities for the years ended 31 December 2018 and 2019 and for the six months ended 30 June 2019 and 2020.

As at 30 June 2020, the Group had accumulated profit and loss account reserves of $16.0 million with balances brought forward of $31.2 million being reduced by losses of $15.2 million incurred in the period. As at 31 December 2019, the Group had accumulated profit and loss account reserves of $31.2 million with balances brought forward of $54.1 million being reduced by losses of $22.8 million incurred in the year. As at 31 December 2018, the Group had accumulated profit and loss account reserves of $54.1 million with balances brought forward of $74.8 million being reduced by losses of $20.7 million incurred in the year.

The Group does not anticipate earning revenues from any of its product candidates before the second half of 2020. The Group anticipates that it will continue to incur losses for the foreseeable future as it continues the development and commercialisation of its products and product candidate and incurs additional costs associated with it being a public listed company.

The Group's principal liquidity needs are to:

- launch BARHEMSYS® and BYFAVO™ in the US by completing additional market research, conducting promotional activities and completion of the building and training of a sales and marketing infrastructure;
- fund its ongoing development activities relating to APD403, including conducting Phase 3 clinical studies for APD403, providing general and administrative support for these operations and protecting the Group's intellectual property; and
- satisfy interest and capital payments under the Hercules Facility and the €25 million Loan Agreement with Cosmo.

The Group's funding requirements will depend on many factors, including but not limited to:

- the ability to successfully commercialise BARHEMSYS® and BYFAVO™ and the rate of adoption of BARHEMSYS® and BYFAVO™ on hospital formularies;
- the cost of establishing and maintaining sales, marketing and distribution capabilities for BARHEMSYS®, BYFAVO™, APD403 (assuming it receives regulatory approval), or any other product candidates for which the Group may receive regulatory approval;
- the amount of sales and other revenues the Group can generate from any approved products, including the sales price and availability of adequate third party reimbursement;
- the initiation, progress, timing, costs and results of clinical trials for APD403;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the effect of competing technological and market developments and the time and cost to respond to them.

From its inception, the Group has funded its operations primarily through placements of equity, raising €38.1 million from the proceeds of the IPO (net of expenses) in March 2018, €10 million from an equity

investment by Cosmo, and £43.0 million (either by way of cash subscription or convertible loans) since its establishment in 2007:

- £3.4 million in November 2017 through the issue of convertible loan notes;
- £4.5 million in December 2016 through the issue of 1,125,000 D preferred shares;
- £10.1 million in July 2015 and February 2016 through the issue of 2,531,250 C preferred shares;
- £2.5 million in February 2015 through the issue of 2,500,833 B preferred shares;
- £5.5 million in June 2014 through the issue of 5,501,832 B preferred shares;
- £7.0 million in August 2013 through the issue of 7,075,396 B preferred shares; and
- £10.0 million in earlier rounds through the issue of 2,664,662 ordinary shares, 3,910,732 S ordinary shares and 9,692,856 A ordinary shares.

The Group has also funded activities through a $10 million term loan facility with Hercules Capital, from which $10 million was drawn on 29 June 2018, and of which $7.8 million was outstanding at 30 June 2020, a €10 million loan facility from Cosmo, which was later terminated and such debt converted into equity, and a €25 million loan facility from Cosmo, the first tranche of which (in the sum of €15 million) the Group drew down on 27 July 2020 and the second tranche of which is available for drawdown until 30 September 2020. The Group has also received £9.8 million in tax credits since its inception.

The Group's principal sources of future liquidity are:

- the proceeds of the Fundraising and any subsequent follow-on equity or debt financing rounds;
- to the extent BARHEMSYS®, BYFAVO™, APD403 or any future products are successfully commercialised, revenues from the sale of such products and revenues from any licence fees, milestone payments and/or royalties resulting from any licensing and/or distribution arrangements in respect of such products entered into by the Group; and
- the €10 million undrawn amount under the €25 million Loan Agreement, which amount is available for drawdown on or before 30 September 2020.

As at 30 June 2020, the Group had cash, cash equivalents and short-term bank deposits of $24.6 million and liabilities of $11.3 million including $7.8 million outstanding under the Hercules Facility. The Group estimates that its net proceeds from the Fundraising will be approximately €22.1 million, after deducting the estimated underwriting commissions and other offering-related fees and expenses payable by the Group.

7.2 Cash flows

The following table sets forth the Group's cash flows for the periods indicated:

Consolidated Cash Flow Statement

	Year ended 31 December 2018 £'000 audited	Year ended 31 December 2018 $'000 unaudited[1]	Year ended 31 December 2019 $'000 audited	Six months ended 30 June 2019 $'000 unaudited	Six months ended 30 June 2020 $'000 unaudited
Net cash used in operating activities	(11,649)	(15,431)	(19,831)	(14,453)	(11,942)
Net cash generated from investing activities	202	246	432	271	39
Net cash generated from financing activities	35,664	48,900	(927)	(560)	19,378
Net increase/(decrease) in cash and cash equivalents	24,217	33,715	(20,326)	(14,742)	7,475
Cash and cash equivalents at end of the period	29,353	37,443	17,009	22,729	24,612

(1) With effect from 1 January 2019, the Group's reporting currency changed from pounds sterling to US dollars. Unless otherwise indicated, sterling amounts presented for the year ended 31 December 2018 have been translated into US dollars using the procedures set forth under the heading "Presentation of financial information" in Part V (*Presentation of Information*).

(a) Net cash used in operating activities

For the six months ended 30 June 2019 and 2020, net cash used in operating activities was $14.5 million and $11.9 million, respectively. Net cash used in operating activities in the six months ended 30 June 2020

and the six months to 30 June 2019 related primarily to expenditure on sales and marketing expenses in undertaking pre-launch activities.

For the years ended 31 December 2018 and 2019, net cash used in operating activities was $15.4 million and $19.8 million, respectively. Net cash used in operating activities in 2019 related primarily to expenditure on sales and marketing expenses in building the commercial infrastructure in the US and undertaking pre-launch activities, together with research and development and administrative expenses, offset by the receipt of R&D tax credits of $0.8 million in respect of the prior year. Net cash used in operating activities in 2018 related primarily to initialising the commercial infrastructure in the US and undertaking pre-launch activities, together with research and development and administrative expenses, offset by the receipt of R&D tax credits of $0.4 million in respect of the prior year. The levels of expenditure varied from period to period principally as a result of the timing and nature of various clinical studies and pre-launch activities. Future research and development activities and commercialisation activities are likely to result in similar fluctuations.

(b) Net cash generated from investing activities

For the six months ended 30 June 2019 and 2020, net cash generated from investing activities was $0.2 million and $0.04 million, respectively. Net cash generated from investing activities in the six months ended 30 June 2020 and the six months ended 30 June 2019 related primarily to interest income on cash and cash equivalents.

For the years ended 31 December 2018 and 2019, net cash generated from investing activities was $0.2 million and $0.4 million, respectively.

(c) Net cash generated from financing activities

For the six months ended 30 June 2019 and 2020, net cash generated from financing activities was $(0.6) million and $19.4 million, respectively. Net cash generated from financing activities in the six months ended 30 June 2020 related primarily to equity investment from Cosmo, offset by loan repayments and interest paid. Net cash used in financing activities in the six months ended 30 June 2019 related primarily to interest paid on the Hercules Facility.

For the years ended 31 December 2018 and 2019, net cash generated from financing activities was $48.9 million and $(0.9) million, respectively. In the year ended 31 December 2019 net cash used in financing activities of $0.9 million was due primarily to interest and fees paid on the Hercules Facility. In the year ended 31 December 2018 net cash generated from financing activities of $48.9 million arose primarily from receipt of approximately $49 million from the gross proceeds of the issuance of ordinary shares as a result of the IPO plus $10 million from the drawdown of the Hercules Facility, offset by repaying the prior Silicon Valley Bank term loan facility.

7.3 Loan facilities

As at 30 June 2020 the Group had $7.8 million outstanding under a term loan facility with Hercules Capital. The Group drew down €15 million on 27 July 2020 under the €25 million Loan Agreement with Cosmo. As at the date of this Prospectus, the remaining €10 million available under the €25 million Loan Agreement is undrawn, and the Group intends to draw down this amount on or before 30 September 2020 for the purposes of its commercialisation strategy.

8. Contractual obligations and commitments

As at 31 December 2018, the Group has committed to certain expenditure in respect of the development of a new 10mg presentation of BARHEMSYS® and in respect of the manufacture of finished product. The commitments amount to $0.5 million in 2018 and $0.4 million in 2019.

As at 30 June 2020, the Group's commitment for leases included a contractual obligation related to the future aggregate minimum amounts payable by the Group under the lease for its office property in Cambridge, England, amounting to $0.02 million, payable within one year, together with commitments under a lease on office premises in Indianapolis which commenced on 1 October 2018 with a term of 5 years and two months, the first two months being rent-free. The annual rent is $112,000.

Payments due but not yet paid to Cosmo under the BYFAVO™ Wind-Up Agreement include: (i) payment of €5 million upon the first commercial sale of BYFAVO™ by the Operating Company, which is expected to be satisfied by the issue of New Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the date of the the first commercial sale of BYFAVO™ by the Operating Company; (ii) US$5 million in cash upon the Operating Company first

achieving US$50 million in annual "net sales" (being gross sales less returns, customary discounts and chargebacks); (iii) US$10 million in cash upon the Operating Company first achieving US$100 million in annual net sales; (iv) US$15 million in cash upon the Operating Company first achieving US$150 million in annual net sales; (v) US$20 million in cash upon the Operating Company first achieving US$200 million in net sales; (vi) US$25 million in cash upon the Operating Company first achieving US$250 million in annual net sales; and (vii) US$30 million in cash upon the Operating Company first achieving US$300 million in annual net sales.

Under the BYFAVO™ Assignment Agreement, royalties on net sales of BYFAVO™ shall also be payable to Paion by the Operating Company of (i) 20 per cent of net sales per calendar year up to a total amount of net sales of US$200 million; (ii) 25 per cent of net sales per calendar year for net sales exceeding US$200 million (on the amount exceeding US$200 million); and (iii) 10 per cent of net sales per calendar year after the expiration of the last-to expire licensed patent and as long as the Operating Company enjoys market exclusivity. Milestones shall also be payable to Paion by the Operating Company of (i) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a second indication; and (ii) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a third indication.

For additional information on the Group's material contracts and summaries thereof, please refer to Part XIV (*Additional Information*).

9. Off-Balance Sheet Arrangements

The Group had no off-balance sheet arrangements, as determined by IFRS, as at 30 June 2020.

10. Dividend Policy

The Company has never declared or paid any cash dividends on its Ordinary Shares. The Company intends to retain future earnings, if any, to finance the operation of its business and does not anticipate paying any cash dividends in the foreseeable future. Any future determination related to the Company's dividend policy will be made at the discretion of the Board after considering its financial condition, results of operations, capital requirements, business prospects and other factors the Board deems relevant, and subject to the restrictions contained in any future financing instruments.

11. Disclosures about Market and Other Risks

The Group's activities expose it to a variety of financial risks including market risk (including currency risk), credit risk, liquidity risk and interest rate cash flow risk. The Group's overall risk management programme focuses on the unpredictability of financial markets and seeks to minimise potential adverse effects on financial performance. The Group does not use derivative financial instruments to hedge risk exposures.

The overall objective of the Board is to set policies that seek to reduce ongoing risk as far as possible without unduly affecting the Group's competitiveness and flexibility. Further details regarding these policies are set out below.

11.1 Credit risk

Credit risk arises primarily from cash and cash equivalents and deposits with banks and financial institutions, as the Group has not yet generated any revenue and so has no trade receivables. Credit risk is managed by ensuring all cash and cash equivalents are deposited with established UK and US banking institutions of high repute and at least an A credit rating.

11.2 Liquidity risk

Liquidity risk arises from the Group's management of working capital and the amount of funding required for the drug development programme and launch of BARHEMSYS®. It is the risk that the Group will encounter difficulty in meeting its financial obligations as they fall due. The Group's policy is to ensure that it will always have sufficient cash to allow it to meet its liabilities when they become due.

The principal liabilities of the Group are the term loans and trade and other payables in respect of the development programme and provision of research services including purchase of laboratory supplies, consumables and related scientific services, as well as sales and marketing costs and administrative costs associated with the Group's business. Trade and other payables are all payable within one month. The Board receives cash flow projections on a regular basis as well as information on cash balances.

11.3 Interest rate cash flow risk

The Group is exposed to interest rate cash flow risk in respect of surplus funds held on deposit. The Directors do not consider this risk to be significant.

The Group is also exposed to some interest rate cash flow in respect of the Hercules Facility as the interest rate is based on the greater of 9.25% or the Wall Street Journal prime rate plus 4.5% The Directors do not consider this risk to be significant.

11.4 Currency risk

Prior to the IPO, the Group conducted substantially all its business in pounds sterling. Since the IPO, the greater proportion of costs have been incurred in US dollars and going forward the Group expects its revenues and costs to be predominantly US dollar-based. To this end, the Group changed its presentational currency from 1 January 2019. The IPO proceeds were transferred into US dollar, sterling and Euro accounts in proportion to the expected currency in which costs would be incurred in 2018 and 2019. Accordingly, the Group has not been exposed to material transactional currency risk, although some translational risks arose upon consolidation.

The Group to date has not hedged its foreign currency exposure, other than holding certain funds in Euro or US dollar accounts to meet known expenditures, since the Directors considered the exposure immaterial. In the future, the Group may enter into currency hedging arrangements, if the Directors believe it to be appropriate.

11.5 Capital risk management

The Group's objectives, when managing capital are to safeguard the Group's ability to continue as a going concern and to maintain an optimal capital structure. Total capital, which is the Group's primary source of funding, is calculated as "Total equity" as shown in the Statement of Financial Position. In order to maintain or adjust the capital structure, the Group may issue new shares or in future adjust the amount of dividends paid to Shareholders or return capital to Shareholders.

The Group had no undrawn committed borrowing facilities available during either of 2019 or 2018.

12. Critical Accounting Policies

The Group's discussion and analysis of its financial condition and results of operations are based on its historical financial information as at and for the years ended 31 December 2018 and 2019, which has been prepared in accordance with IFRS as adopted by the European Union. A summary of the Group's significant accounting policies is set forth in note 1 in the 2019 Annual Financial Statements incorporated by reference into this Prospectus.

The preparation of this financial information requires the Group to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities in the Group's financial information. The Group bases its estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates.

The Directors believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of its consolidated financial information. On an ongoing basis, the Group evaluates its estimates and judgments, including those related to accrued expenses and share-based compensation. Revisions to accounting estimates are recognised in the period in which the estimates are revised if the revision affects only that period or in the period of revision and future periods if the revision affects both current and future periods.

Information about critical judgments in applying accounting policies that had the most significant effect on amounts recognised in the consolidated financial statements of the Group during the period under review is set out below.

Compound Financial Instruments

In 2018, compound financial instruments issued by the Group comprised convertible shares that can be converted to share capital at the option of the holder, and the number of shares to be issued does not vary with changes in their fair value. The Group's A Ordinary shares and B Preferred shares and C Preferred shares were classified as compound financial instruments.

The liability component of the compound financial instrument is recognised initially at the fair value of a similar liability that does not have an equity conversion option. The equity component is recognised initially at the difference between the fair value of the compound financial instrument as a whole and the fair value of the liability component. Any directly attributable transaction costs are allocated to the liability and equity components in proportion to their initial carrying amounts.

Subsequent to initial recognition, the liability component of a compound financial instrument is measured at amortised cost using the effective interest method. The equity component of a compound financial instrument is not re-measured subsequently to initial recognition except on conversion or expiry.

Where the terms of financial instruments are amended such that there is a substantial change in expected future cash flows, the financial instrument is treated as extinguished and re-issued giving rise to a gain or loss on extinguishment. The gain or loss on extinguishment is calculated as the difference between the fair value of the instrument immediately prior to the extinguishment and the fair value of the replaced instrument. The gain or loss is allocated to equity in the year of extinguishment.

Term Loans and Convertible Loan Notes

In 2017, the Group entered into a term loan and issued convertible loan notes. These were measured at amortised cost using the effective interest rate method.

The convertible loan notes and convertible shares were converted into Ordinary Shares in the Group immediately prior to the IPO on 6 March 2018.

The term loan was repaid in full on 27 June 2018.

The Hercules Facility, a new term loan facility, was drawn on 29 June 2018. The initial tranche drawn was $10 million and costs of $644 thousand were incurred. The loan bears interest at the higher of 9.5 per cent or the Wall Street Journal prime rate plus 4.5 per cent, bears a final payment charge of 3.95 per cent of the principal, and was interest only until January 2020. Thereafter the principal and interest on the loan are repayable in 25 equal monthly instalments. Warrants over 201,330 Ordinary Shares, exercisable at €3.22 per share, were issued to the lender as part of the terms of the loan facility.

The Group drew down €15 million on 27 July 2020 under the €25 million Loan Agreement with Cosmo. As at the date of this Prospectus, the remaining €10 million available under the €25 million Loan Agreement is undrawn, which amount will be available for drawdown on or before 30 September 2020. The Group intends to drawn down the remaining amount for the purposes of its commercialisation strategy. The €25 million Loan Agreement is unsecured and subordinated to the Hercules Facility. Interest will accrue daily on the amount drawn and be payable monthly at the rate of 11 per cent per annum until the Company has discharged the Hercules Facility. Once security is released under the Hercules Facility, certain security, including fixed and floating charges over all or substantially all of the assets of each member of the Group, will be pledged under the €25 million Loan Agreement and interest will be reduced to 9 per cent per annum. The loan will be repayable in 24 equal monthly instalments commencing in July 2023. Interest shall accrue daily from the date of drawdown, and be payable monthly.

PART XI

HISTORICAL FINANCIAL INFORMATION

1. Introduction

The audited consolidated financial statements for the Company for the year ended 31 December 2019 (the "**2019 Annual Financial Statements**") and the audited consolidated financial statements for the Company for the year ended 31 December 2018 (the "**2018 Annual Financial Statements**") have been prepared in accordance with IFRS. The 2019 Annual Financial Statements and the 2018 Annual Financial Statements, in respect of which the Company's auditors, PricewaterhouseCoopers LLP, made unqualified reports under section 495 and 497 of the Companies Act, did not contain any statement under section 498(2) or (3) of that Act.

The unaudited consolidated financial statements for the Company for the six months ended 30 June 2020 (the "**2020 Interim Financial Statements**") have been prepared in accordance with IAS 34 Interim Financial Reporting. They do not contain all of the information which IFRS would require for a complete set of financial statements and should be read in conjunction with the 2019 Annual Financial Statements.

The 2020 Interim Financial Statements were prepared on the basis that the Group, in order to continue as a going concern, would not increase its cost base as planned (for the commercialisation of BARHEMSYS® or BYFAVO™) if the Group were unable to obtain debt or equity financing. The Fundraising, pursuant to which the Company has raised net proceeds of approximately €22.1 million, constitutes such an equity financing and the proceeds of the Fundraising allow the Group to proceed with its plans to commercialise BARHEMSYS® and BYFAVO™ while continuing as a going concern. However additional funding will be required in the fourth quarter of 2021.

The Fundraising is being underwritten by the Banks, subject to the terms and conditions set out in the Placing Agreement, including Admission occurring no later than 18 August 2020 (or such later date as the Company and the Banks may agree). To the extent that any placee procured by the Banks fails to subscribe for any or all of the New Ordinary Shares allotted to it, the Banks shall themselves subscribe for such New Ordinary Shares at the Placing Price. In such circumstances, each Bank shall be required to subscribe for such New Ordinary Shares at the Placing Price only in respect of the placees it has procured.

In the unlikely event that the Fundraising does not proceed to completion and/or Admission does not occur as provided for in the Placing Agreement, the Directors believe that the Group can continue as a going concern, but the Group's plans to commercialise BARHEMSYS® or BYFAVO™ would be dependent on the Group obtaining alternative forms of financing. In those circumstances, the Directors consider that such alternative forms of financing following a scaled back launch of its products should be available to the Group in the form of additional debt facilities, receivables factoring and/or synthetic royalty type arrangements, albeit any such alternative financing arrangements would likely be on terms that would have a detrimental effect on the Group's expected financial position.

The Directors are confident that it was appropriate to prepare the 2020 Interim Financial Statements on the going concern basis. However, there is no guarantee that attempts to raise adequate additional financing on a timely basis will be successful and therefore this represents a material uncertainty, which may cast significant doubt about the Group's ability to continue as a going concern. The 2020 Interim Financial Statements do not include the adjustments that would result if the Group were unable to continue as a going concern.

2. Historical financial information

The parts of the Company's published interim report and unaudited financial statements for the six months ended 30 June 2020, annual report and audited financial statements of the Company for the year ended 31 December 2019 and annual report and audited financial statements of the Company for the year ended 31 December 2018 set out in the table below are expressly incorporated by reference into this document. The non-incorporated parts of the interim report and financial statements and annual report and financial statements are either not relevant to investors or are covered elsewhere in this document. The incorporated parts of the interim report and financial statements and annual report and financial statements should be read in conjunction with Part VI (*Information on the Company and the Group*), Part X (*Operating and Financial Review*) and Part II (*Risk Factors*).

The incorporated parts of these documents (which have previously been filed with, or notified to, the FCA) are available for inspection as set forth in Section 23 of Part XIV (*Additional Information*) and are also available on the Company's website using the following hyperlinks:

(a) interim report and unaudited consolidated financial statements for the six months ended 30 June 2020: https://www.acaciapharma.com/files/download/179;

(b) annual report and audited consolidated financial statements for the year ended 31 December 2019: https://www.acaciapharma.com/files/download/172; and

(c) annual report and audited consolidated financial statements for the year ended 31 December 2018: https://www.acaciapharma.com/files/download/158.

Nature of information	Audited annual report and financial statements for the year ended 31 December 2018 Page No. (s)	Audited annual report and financial statements for the year ended 31 December 2019 Page No. (s)	Unaudited interim report and financial statements for the six months ended 30 June 2020 Page No. (s)
Independent auditor's report	50-56	55-60	—
Consolidated income statement	57	61	—
Consolidated statement of comprehensive income	57	61	6
Consolidated statement of financial position	58	62	7
Consolidated cash flow statement	59	63	8
Consolidated statement of changes in equity	60	64	9
Notes to the Group's financial statements	61-79	65-87	10-16
Company's statement of financial position	81	89	—
Company's statement of changes in equity	82	90	—
Notes to the Company's financial statements	83-87	91-96	—
Independent review report	—	—	17-18

To the extent that any document or information incorporated by reference or attached to this Prospectus itself incorporates any information by reference, either expressly or impliedly, such information will not form part of this Prospectus for the purposes of the Prospectus Regulation Rules, except where such information or documents are stated within this document as specifically being incorporated by reference or where this Prospectus is specifically defined as including such information.

Any statement contained in a document which is deemed to be incorporated by reference into this Prospectus shall be deemed to be modified or superseded for the purpose of this Prospectus to the extent that a statement contained in this Prospectus (or in a later document which is incorporated by reference into this Prospectus) modifies or supersedes such earlier statement (whether expressly, by implication or otherwise). Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Prospectus.

PART XII

DETAILS OF THE FUNDRAISING

1. ORDINARY SHARES SUBJECT TO THE FUNDRAISING

The Fundraising comprises the subscription of 12,500,000 New Ordinary Shares to be issued by the Company, raising approximately €22.1 million (net of commissions, fees and expenses).

Following the issue of the New Ordinary Shares to be allotted pursuant to the Fundraising, Shareholders will suffer dilution to their proportionate ownership and voting rights of approximately 14.7 per cent to their interests in the Company immediately prior to the Fundraising.

2. THE FUNDRAISING

The Fundraising is being made by way of subscriptions for the New Ordinary Shares by: (i) certain institutional and professional investors in the United Kingdom and Belgium and elsewhere outside the United States in reliance on Regulation S; and (ii) in the United States to persons reasonably believed to be QIBs.

Certain restrictions that apply to the distribution of this Prospectus and the offer and issue of the New Ordinary Shares in jurisdictions outside the UK are described below in Section 12 of this Part XII (*Details of the Fundraising*).

The Fundraising is subject to satisfaction of conditions which are customary for transactions of this type as set out in the Placing Agreement, including, amongst others, Admission of the New Ordinary Shares and the Placing Agreement not having been terminated in accordance with its terms.

When admitted to trading, the New Ordinary Shares will be registered with ISIN GB00BYWF9Y76 and will be traded in Euros under the ticker symbol ACPH. The Company's LEI code is 213800SLDKXWKT6E3381.

The New Ordinary Shares being issued pursuant to the Fundraising will, on their Admission, rank *pari passu* in all respects with the Existing Ordinary Shares and will rank in full for all dividends and other distributions thereafter declared, made or paid on the share capital of the Company. The New Ordinary Shares will, immediately on and from their Admission, be freely transferable, subject to the Articles. The rights attaching to the New Ordinary Shares will be uniform in all respects and they will form a single class for all purposes.

The Company, the Directors, and the Banks expressly reserve the right to determine, at any time prior to Admission of the New Ordinary Shares, not to proceed with the Fundraising. If such right is exercised, the Fundraising will lapse and any monies received in respect of the Fundraising will be returned to investors without interest.

There are no material conflicts of interest pertaining to the Fundraising or Admission.

3. REASONS FOR THE FUNDRAISING AND USE OF PROCEEDS

The net proceeds payable to the Company from the Fundraising will be approximately €22.1 million (after deducting underwriting commissions and other offering-related fees and expenses plus VAT thereon, if applicable, of approximately €2.9 million).

The net proceeds of the Fundraising, together with the Group's existing cash resources and loan facilities, are expected to allow the Group to complete the establishment of its sales and marketing infrastructure, to launch BARHEMSYS® and BYFAVO™ to the hospital market in the US in late-2020 and to promote the products until the fourth quarter of 2021.

The Company intends to apply the net proceeds it receives from the Fundraising as follows:

(a) recruit an initial sales force of approximately 30, with an additional ten support staff;

(b) pay marketing costs relating to BARHEMSYS® and BYFAVO™ including brand development and engagement (both virtually and, where possible, in person) with key opinion leaders, healthcare professionals and medical conference and speaker programmes;

(c) implement post-approval research and development commitments including paediatric studies for BARHEMSYS® and BYFAVO™ and a renal study for BARHEMSYS®;

(d) satisfy interest and capital payments under existing loan agreements; and

(e) general corporate purposes relating to ongoing commercial activities as well as supplementing existing stock of both BARHEMSYS® and BYFAVO™.

4. WITHDRAWAL RIGHTS

If the Company is required to publish any supplementary prospectus, applicants who have applied for New Ordinary Shares under the Fundraising shall have at least two clear business days following the publication of the relevant supplementary prospectus within which to withdraw their application to acquire New Ordinary Shares in its entirety. The right to withdraw an application to acquire New Ordinary Shares in these circumstances will be available to all investors under the Fundraising. If the application is not withdrawn within the stipulated period, any application to apply for New Ordinary Shares under the Fundraising will remain valid and binding.

Details of how to withdraw an application will be made available if a supplementary prospectus is published.

5. ALLOCATIONS UNDER THE FUNDRAISING

The allocation of New Ordinary Shares among prospective investors has been determined by the Banks and the Company. All New Ordinary Shares issued pursuant to the Fundraising will be issued, payable in full, at the Placing Price, as applicable. No commissions, fees, expenses or taxes will be charged to investors by the Company under the Fundraising.

Upon accepting any allocation, prospective investors will be contractually committed to acquire the number of New Ordinary Shares allocated to them at the Placing Price and, to the fullest extent permitted by law, will be deemed to have agreed not to exercise any rights to rescind or terminate, or otherwise withdraw from such commitment. Dealing may not begin before notification is made. A number of factors have been considered in determining the Placing Price and the basis of allocation, including the prevailing market conditions, the level and nature of demand for the New Ordinary Shares, the prices bid to acquire the New Ordinary Shares and the objective of establishing an orderly and liquid after-market in the Ordinary Shares. The Placing Price and the number of New Ordinary Shares to be issued pursuant to the Fundraising have been established at a level determined in accordance with these arrangements, taking into account indications of interest received from prospective investors.

6. PLACING ARRANGEMENTS

The Company, the Directors and the Banks have entered into the Placing Agreement pursuant to which, on the terms and subject to certain conditions contained therein (which are customary in agreements of this nature), Jefferies and Guggenheim Securities have agreed, as agents for the Company, severally to use reasonable endeavours to procure placees for the New Ordinary Shares within the United States, the United Kingdom and elsewhere outside the European Union and Jefferies and Degroof Petercam have agreed, as agents for the Company, severally to use reasonable endeavours to procure placees for the New Ordinary Shares in the United States, the European Union and the United Kingdom. Bank Degroof Petercam SA/NV is not a US-registered broker-dealer; therefore, to the extent that it intends to effect any sales of the shares in the United States, it will do so through Global Alliance Securities, LLC, its affiliated US-registered broker-dealer, in accordance with the SEC Rule 15a-6, and as permitted by FINRA regulations. The Fundraising is being underwritten by the Banks, subject to the terms and conditions set out in the Placing Agreement. To the extent that any placee procured by the Banks fails to subscribe for any or all of the New Ordinary Shares allotted to it, the Banks shall themselves subscribe for such New Ordinary Shares at the Placing Price. In such circumstances, each Bank shall be required to subscribe for such New Ordinary Shares at the Placing Price only in respect of the placees it has procured.

Commitments under the Fundraising are conditional upon, *inter alia*, Admission of the New Ordinary Shares occurring not later than 8:00 a.m. CET on 18 August 2020 (or such later date or time as the Banks and the Company may agree) and the Placing Agreement becoming unconditional in all respects and not having been terminated in accordance with its terms.

The Placing Agreement provides for the Banks to be paid a commission in respect of the New Ordinary Shares sold. Any commissions received by the Banks may be retained and any New Ordinary Shares acquired by them may be retained or dealt in by them for their own benefit.

All New Ordinary Shares issued pursuant to the Fundraising will be issued at the Placing Price. Liability for UK stamp duty and SDRT and Belgian tax considerations are described in Part XIII (*Taxation*).

Further details of the terms of the Placing Agreement are set out in Part XIV (*Additional Information*).

7. ADMISSION OF THE NEW ORDINARY SHARES

Application will be made for the New Ordinary Shares to be admitted to trading on the regulated market of Euronext Brussels. The New Ordinary Shares will be traded in Euros under trading symbol "ACPH" with ISIN code GB00BYWF9Y76. No application has been or will be made for admission of the New Ordinary Shares to trading on any other stock exchange.

8. LOCK-UP ARRANGEMENTS

On 11 August 2020, each of the Directors, Senior Managers and Cosmo entered into a Lock-Up Agreement. Under the terms of the Lock-Up Agreements, each of the Directors, Senior Managers and Cosmo has agreed that, subject to certain exceptions, during the period commencing on the date of Admission and ending on the date 90 days from the date of Admission, he or it will not, without the prior written consent ofJefferies and Guggenheim Securities, (a) offer, sell, assign, transfer, contract to offer, sell, assign, transfer, pledge (unless such pledged shares cannot be sold within the 90 day period referred to above) or otherwise transfer or dispose of, directly or indirectly, any Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares or warrants or other rights to subscribe for Ordinary Shares, or enter into any derivative or other transaction having substantially similar economic effect with respect to the Ordinary Shares or any such securities or (b) announce publicly its intention to do any of the foregoing.

Pursuant to the Placing Agreement, the Company has agreed that during the period of 90 days from the date of Admission, it will not without the prior written consent of Jefferies and Guggenheim Securities, (a) directly or indirectly, issue, offer, allot, lend, sell, contract to sell or issue, grant any option, right or warrant to subscribe or purchase or allow any Encumbrance to be created over or otherwise dispose of, directly or indirectly, any Shares (or any securities convertible into or exchangeable for Shares or which carry rights to subscribe or purchase Shares) or any interest (within the meaning of section 820 of CA 2006) in any Shares or enter into any transaction with the same economic effect as, or agree to do, any of such things; or (b) publicly announce any intention to do any of such things.

9. DEALING ARRANGEMENTS

Applications have been or will be made for all of the New Ordinary Shares to be admitted to trading on the regulated market of Euronext Brussels. Trading of the New Ordinary Shares on the regulated market of Euronext Brussels is expected to commence, on an "if-and-when-issued-or-delivered" basis, on or about 18 August 2020. Delivery of the New Ordinary Shares is expected to take place in book-entry form on or about 18 August 2020. The above-mentioned dates and times may be subject to change without further notice.

Each investor will be required to undertake to pay the Placing Price for the New Ordinary Shares issued to such investor in such manner as shall be directed by the Banks.

It is intended that, where applicable, definitive share certificates in respect of the New Ordinary Shares will be despatched by 28 August 2020 or as soon thereafter as is practicable. Temporary documents of title will not be issued. Dealings in advance of crediting of the investors securities account(s) shall be at the sole risk of the persons concerned.

10. EUROCLEAR BELGIUM

All New Ordinary Shares will be delivered in book-entry form, and will be credited to investors' securities accounts via Euroclear Belgium, the Belgian central securities depository, Koning Albert II laan 1, 1210 Brussels, Belgium.

11. CONDITIONALITY OF THE FUNDRAISING

The Fundraising is subject to the satisfaction of conditions which are customary for transactions of this type contained in the Placing Agreement, including Admission of the New Ordinary Shares becoming effective by no later than 8:00 a.m. CET on 18 August 2020 (or such later date as the Banks and the Company may agree) and the Placing Agreement not having been terminated prior to such Admission. See Section 6 of this Part XII (*Details of the Fundraising*) for further details about the placing arrangements.

12. SELLING AND TRANSFER RESTRICTIONS

The distribution of this Prospectus and the offer of the New Ordinary Shares in certain jurisdictions may be restricted by law and therefore persons into whose possession this Prospectus comes should inform themselves about and observe any restrictions, including those set out in the paragraphs that follow. Any failure to comply with these restrictions may constitute a violation of the securities laws of any such jurisdiction.

No action has been or will be taken in any jurisdiction that would permit a public offering of the New Ordinary Shares, or possession or distribution of this Prospectus or any other offering material in any country or jurisdiction where action for that purpose is required. Accordingly, the New Ordinary Shares may not be offered or sold, directly or indirectly, and neither this Prospectus nor any other offering material or advertisement in connection with the New Ordinary Shares may be distributed or published in or from any country or jurisdiction except in circumstances that will result in compliance with any and all applicable rules and regulations of any such country or jurisdiction. Persons into whose possession this Prospectus comes should inform themselves about and observe any restrictions on the distribution of this Prospectus and the offer of the New Ordinary Shares contained in this Prospectus. Any failure to comply with these restrictions may constitute a violation of the securities laws of any such jurisdiction. This Prospectus does not constitute an offer to subscribe for or purchase any of the New Ordinary Shares to any person in any jurisdiction to whom it is unlawful to make such offer or solicitation in such jurisdiction.

12.1 *European Economic Area*

In relation to each Member State of the European Economic Area and the United Kingdom (each a "Relevant State") no New Ordinary Shares have been offered or will be offered pursuant to the Fundraising to the public in that Relevant State prior to the publication of a prospectus in relation to the New Ordinary Shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that an offer to the public in that Relevant State of any New Ordinary Shares may be made at any time under the following exemptions under the Prospectus Regulation:

(a) to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Regulation); or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of New Ordinary Shares shall require the Company or any Bank to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to any Ordinary Shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the Fundraising and any New Ordinary Shares to be offered so as to enable an investor to decide to purchase or subscribe for any New Ordinary Shares and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

In the case of any New Ordinary Shares being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, such financial intermediary will also be deemed to have represented, acknowledged and agreed that the New Ordinary Shares acquired by it in the Fundraising have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise of an offer of any New Ordinary Shares to the public other than their offer or resale in a Relevant State to "qualified investors" within the meaning of Article 2(e) of the Prospectus Regulation or in circumstances in which the prior consent of the Banks has been obtained to each such proposed offer or resale. The Company, the Banks and their respective affiliates, and others will rely upon the truth and accuracy of the foregoing representation, acknowledgement and agreement. Notwithstanding the above, a person who is not a qualified investor and who has notified the Banks of such fact in writing may, with the prior consent of the Banks, be permitted to acquire New Ordinary Shares in the Fundraising.

12.2 *United States*

This Prospectus is not a public offering (within the meaning of the Securities Act) of securities in the US. The New Ordinary Shares have not been and will not be registered under the Securities Act or with any

securities regulatory authority of any state or other jurisdiction of the US and may not be offered or sold in the US except in transactions exempt from, or not subject to, the registration requirements of the Securities Act and in accordance with any applicable securities laws of any state or other jurisdiction of the US. Accordingly, the Banks may offer New Ordinary Shares (i) in the US to persons reasonably believed to be QIBs, or (ii) outside the US in offshore transactions to non-US persons in reliance on Regulation S.

In addition, until 40 days after the commencement of the Fundraising, any offer or sale of New Ordinary Shares within the US by any dealer (whether or not participating in the Fundraising) may violate the registration requirements of the Securities Act if such offer or sale is made otherwise than in accordance with an available exemption from registration under the Securities Act.

12.3 *Purchasers in the United States*

Each purchaser of New Ordinary Shares within the US, by accepting delivery of this Prospectus and the New Ordinary Shares, will be deemed to have represented, agreed and acknowledged that:

(a) the purchaser has such knowledge and experience in financial and business matters that the purchaser is capable of evaluating the merits and risks of an investment in the New Ordinary Shares and are authorized to consummate the purchase of the New Ordinary Shares in compliance with all applicable laws an regulations;

(b) the purchaser is, and at the time of its purchase of any New Ordinary Shares will be, a QIB within the meaning of Rule 144A;

(c) the purchaser understands and acknowledges that the New Ordinary Shares have not been and will not be registered under the Securities Act or with any securities regulatory authority of any state or other jurisdiction of the US and is aware, and each purchaser and beneficial owner of such New Ordinary Shares has been advised, that sellers of the New Ordinary Shares may be relying on Rule 144A or another exemption from the registration requirements of Section 5 of the Securities Act;

(d) the purchaser is purchasing the New Ordinary Shares (i) for its own account, or (ii) for the account of one or more other QIBs with respect to which it is acting as duly authorised fiduciary or agent with sole investment discretion and on behalf of which it has full authority to make, and does make, the acknowledgments, representations and agreements herein, in each case for investment purposes and not with a view to any resale or distribution of any such New Ordinary Shares;

(e) the purchaser understands and agrees that offers and sales of the New Ordinary Shares are being made in the US only to QIBs in transactions not involving a public offering which are exempt from the registration requirements of the Securities Act, and that if in the future it decides to offer, sell, pledge, or otherwise transfer any New Ordinary Shares, it will do so only (i) to a person that it and any person acting on its behalf reasonably believes is a QIB purchasing for its own account or the account of another QIB in a transaction meeting the requirements of Rule 144A, (ii) in an "offshore transaction" in accordance with Rule 903 or Rule 904 of Regulation S or (iii) pursuant to the exemption from the registration requirements of the Securities Act provided by Rule 144 thereunder (if available) and, in each case, in accordance with any applicable securities laws of any state or other jurisdiction of the US and of any other jurisdiction. The purchaser understands that no representation can be made as to the availability of the exemptions provided by Rule 144A or Rule 144 under the Securities Act for the resale of the New Ordinary Shares;

(f) the purchaser understands that any offer, sale, pledge or other transfer made other than in compliance with the above stated restrictions may not be recognised by the Company;

(g) the purchaser agrees that it will give to each person to whom it transfers New Ordinary Shares notice of any restrictions on transfer of such New Ordinary Shares;

(h) the purchaser understands that for so long as the New Ordinary Shares are "restricted securities" within the meaning of Rule 144(a)(3) under the Securities Act, no such New Ordinary Shares may be deposited into any unrestricted depositary receipt facility established or maintained by a depositary bank;

(i) the purchaser understands that the New Ordinary Shares (to the extent they are in certificated form), unless otherwise determined by the Company in accordance with applicable law, will bear a legend substantially to the effect set out in Section 13 (*Transfer Restrictions*) hereof;

(j) taking the foregoing into consideration, in making a decision to purchase New Ordinary Shares, the purchaser agrees that it has not received or relied on any communication, investment advice or

recommendation from the Company or any of its affiliates or advisors (including the Banks) and (i) has made its own assessment of the relevant tax, legal, economic and other investment risks independently with regard to its investment decision with respect to the New Ordinary Shares, (ii) has exercised independent judgment in evaluating the recommendations of any broker dealer or US associated person, and (iii) confirms that it has undertaken an independent analysis of the merits and risks of an investment in the New Ordinary Shares, based on its own financial circumstances. The purchaser further represents that it will be relying on the information to be found in this Prospectus in making its own independent investment decision with respect to the purchase of New Ordinary Shares; and

(k) the purchaser understands that these representations and undertakings are required in connection with the securities laws of the US and that the Company, the Banks, their respective affiliates and others will rely upon the truth and accuracy of the foregoing acknowledgements, representations and agreements, and agrees that, if any of such representations, agreements or acknowledgments deemed to have been made by virtue of its purchase of New Ordinary Shares are no longer accurate, it will promptly notify the Company and if it is acquiring any New Ordinary Shares as a fiduciary or agent for one or more accounts, it represents that it has sole investment discretion with respect to each such account and that it has full power and authority to make, and does make, the foregoing representations, agreements and acknowledgments on behalf of each such account.

12.4 *Purchasers pursuant to Regulation S*

Each purchaser who acquires New Ordinary Shares pursuant to Regulation S, by accepting delivery of this Prospectus and the New Ordinary Shares, will be deemed to have represented, agreed and acknowledged that:

(a) the purchaser understands that the New Ordinary Shares have not been and will not be registered under the Securities Act or with any securities regulatory authority of any state or other jurisdiction of the United States;

(b) the purchaser is purchasing such New Ordinary Shares in an offshore transaction meeting the requirements of Regulation S;

(c) the purchaser is not an affiliate of the Company or a person acting on behalf of such an affiliate;

(d) the purchaser will not offer, sell, pledge or transfer any New Ordinary Shares except in accordance with the Securities Act and any applicable laws of any state or other jurisdiction of the United States and any other jurisdiction;

(e) the purchaser is not a "US person" as defined in Regulation S; and

(f) the purchaser understands that the Company and the Banks, their respective affiliates and others will rely upon truth and accuracy of the foregoing acknowledgements, representations and agreements, agrees that, if any of such representations, agreements or acknowledgments deemed to have been made by virtue of its purchase of New Ordinary Shares are no longer accurate, it will promptly notify the Company and if it is acquiring any New Ordinary Shares as a fiduciary or agent for one or more accounts, it represents that it has sole investment discretion with respect to each such account and that it has full power and authority to make, and does make, the foregoing representations, agreements and acknowledgments on behalf of each such account.

12.5 *Japan*

The New Ordinary Shares have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended; the "**FIEA**"). The New Ordinary Shares may not be offered or sold directly or indirectly, in Japan or to, or for the benefit of, any resident in Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organised under the laws of Japan), or to others for reoffering or resale, directly or indirectly, in Japan or to, or for the benefit of, a resident of Japan except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEA and any other applicable laws, regulations and ministerial guidelines of Japan.

12.6 *Australia*

This Prospectus does not constitute a prospectus or other disclosure document under the Corporations Act 2001 (Cth) Australia ("**Corporations Act**") and does not purport to include the information required of a disclosure document under the Corporations Act. This document has not been, and will not be, lodged

with the Australian Securities and Investments Commission (whether as a disclosure document under the Corporations Act or otherwise). Any offer of in Australia of the New Ordinary Shares under this Prospectus or otherwise may only be made to persons who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), to "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions under section 708 of the Corporations Act so that it is lawful to offer the New Ordinary Shares in Australia without disclosure to investors under Part 6D.2 of the Corporations Act.

Any offer for on-sale of the New Ordinary Shares that is received in Australia within 12 months after their issue by the Company is likely to need prospectus disclosure to investors under Part 6D.2 of the Corporations Act, unless such offer for on-sale in Australia is conducted in reliance on a prospectus disclosure exemption under section 708 of the Corporations Act or otherwise. Any persons acquiring New Ordinary Shares should observe such Australian on-sale restrictions.

The Company and the Banks are not licensed in Australia to provide financial product advice in relation to the New Ordinary Shares. Any advice contained in this document is general advice only. This document has been prepared without taking account of any investor's objectives, financial situation or needs, and before making an investment decision on the basis of this document, investors should consider the appropriateness of the information in this document, having regard to their own objectives, financial situation and needs.

12.7 *Canada*

The New Ordinary Shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the New Ordinary Shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities laws in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this Prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities laws of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the Banks are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

12.8 *Singapore*

This Prospectus has not been and will not be registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this Prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of New Ordinary Shares may not be circulated or distributed, nor may the New Ordinary Shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "**SFA**"), (ii) to a relevant person pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where New Ordinary Shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

securities or securities-based derivatives contracts (each as defined in the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the New Ordinary Shares pursuant to an offer made under Section 275 of the SFA except:

(c) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(d) where no consideration is or will be given for the transfer;

(e) where the transfer is by operation of law; or

(f) as specified in Section 276(7) of the SFA.

12.9 *Switzerland*

The New Ordinary Shares may not be publicly offered into or in Switzerland and will not be listed on the SIX Swiss Exchange ("**SIX**") or on any other stock exchange or regulated trading facility in Switzerland. This Prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland and therefore do not constitute an issuance prospectus within the meaning of the Swiss Code of Obligations or a listing prospectus within the meaning of the SIX listing rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this Prospectus nor any other offering or marketing material relating to the New Ordinary Shares may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this Prospectus nor any other offering or marketing material relating to the offering, the Company or the New Ordinary Shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this Prospectus will not be filed with, and the offer of New Ordinary Shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of New Ordinary Shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("**CISA**"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of New Ordinary Shares.

12.10 *South Africa*

The New Ordinary Shares may not be and, accordingly, are not being offered or sold to prospective investors in the Republic of South Africa. Accordingly, the offer of the New Ordinary Shares will not constitute a public offer as defined in Section 96 of the Companies Act, 2008 (as amended) (the "**Companies Act**") and this document does not, nor is it intended to, constitute a Prospectus prepared and registered under the Companies Act.

12.11 *Jersey*

No person may circulate in Jersey any offer for subscription, sale or exchange of any of the New Ordinary Shares.

12.12 *Other overseas territories*

Investors in jurisdictions other than the European Economic Area, the US, Japan, Australia and Canada should consult their professional advisers as to whether they require any governmental or other consents or need to observe their formalities to enable them to purchase any New Ordinary Shares under the Fundraising.

13. TRANSFER RESTRICTIONS

13.1 *Purchasers in the United States*

(a) If in the future any US purchaser decides to offer, sell, pledge, or otherwise transfer any New Ordinary Shares, it will do so only (i) to a person that it and any person acting on its behalf reasonably believes is a QIB purchasing for its own account or the account of another QIB, (ii) in an "offshore transaction" in accordance with Rule 903 or Rule 904 of Regulation S or (iii) pursuant to the exemption from the registration requirements of the Securities Act provided by Rule 144 thereunder (if available) and, in each case, in accordance with any applicable securities laws of any state or other jurisdiction of the US and of any other jurisdiction. The purchaser understands that no

representation can be made as to the availability of the exemptions provided by Rule 144A or Rule 144 under the Securities Act for the resale of the New Ordinary Shares.

(b) The purchaser understands that the New Ordinary Shares (to the extent they are in certificated form), unless otherwise determined by the Company in accordance with applicable law, will bear a legend substantially to the following effect:

THE NEW ORDINARY SHARES REPRESENTED HEREBY HAVE NOT BEEN AND WILL NOT BE REGISTERED UNDER THE US SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT") OR WITH ANY SECURITIES REGULATORY AUTHORITY OF ANY STATE OR OTHER JURISDICTION OF THE US AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT (1) TO A PERSON THAT THE SELLER AND ANY PERSON ACTING ON ITS BEHALF REASONABLY BELIEVES IS A QUALIFIED INSTITUTIONAL BUYER WITHIN THE MEANING OF RULE 144A UNDER THE SECURITIES ACT PURCHASING FOR ITS OWN ACCOUNT OR FOR THE ACCOUNT OF ANOTHER QUALIFIED INSTITUTIONAL BUYER, (2) IN AN OFFSHORE TRANSACTION IN ACCORDANCE WITH RULE 903 OR RULE 904 OF REGULATION S UNDER THE SECURITIES ACT OR (3) PURSUANT TO THE EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE SECURITIES ACT PROVIDED BY RULE 144 THEREUNDER (IF AVAILABLE) AND, IN EACH CASE, IN ACCORDANCE WITH ANY APPLICABLE SECURITIES LAWS OF ANY STATE OR OTHER JURISDICTION OF THE US AND OF ANY OTHER JURISDICTION. NO REPRESENTATION CAN BE MADE AS TO THE AVAILABILITY OF THE EXEMPTIONS PROVIDED BY RULE 144A OR RULE 144 UNDER THE SECURITIES ACT FOR RESALES OF THE NEW ORDINARY SHARES. NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THE FOREGOING, THE ORDINARY SHARES REPRESENTED HEREBY ARE "RESTRICTED SECURITIES" WITHIN THE MEANING OF RULE 144(a)(3) UNDER THE SECURITIES ACT AND FOR SO LONG AS SUCH SECURITIES ARE "RESTRICTED SECURITIES" (AS SO DEFINED), THE SECURITIES MAY NOT BE DEPOSITED INTO ANY UNRESTRICTED DEPOSITARY RECEIPT FACILITY IN RESPECT OF THE ORDINARY SHARES ESTABLISHED OR MAINTAINED BY A DEPOSITARY BANK. EACH HOLDER, BY ITS ACCEPTANCE OF ORDINARY SHARES, REPRESENTS THAT IT UNDERSTANDS AND AGREES TO THE FOREGOING RESTRICTIONS.

PART XIII

TAXATION

A. UK TAXATION

*The following statements are intended only as a general guide to certain UK tax considerations relevant to prospective investors in the Ordinary Shares. They do not purport to be a complete analysis of all potential UK tax consequences of acquiring, holding or disposing of Ordinary Shares. They are based on current UK tax law and what is understood to be the current practice (which may not be binding) of HM Revenue and Customs ("**HMRC**") as at the date of this Prospectus, both of which are subject to change, possibly with retrospective effect. The following statements relate only to Shareholders who are resident (and, in the case of individuals, resident and domiciled) for tax purposes in (and only in) the UK (except insofar as express reference is made to the treatment of non-UK residents or non-UK domiciled Shareholders), who hold their Ordinary Shares as an investment (other than under an individual savings account or self-invested personal pension arrangement) and who are the absolute beneficial owners of both the Ordinary Shares and any dividends paid on them. The tax position of certain categories of Shareholders who are subject to special rules, such as (but not limited to) persons who acquire (or are deemed to acquire) their Ordinary Shares in connection with their (or another person's) office or employment, traders, brokers, dealers in securities, insurance companies, banks, financial institutions, investment companies, tax-exempt organisations, persons connected with the Company or the Group, persons holding Ordinary Shares as part of hedging or conversion transactions, Shareholders who are not domiciled or not resident in the UK, collective investment schemes, trusts and those who hold 5 per cent or more of the Ordinary Shares, is not considered. Nor do the following statements consider the tax position of any person holding investments in any HMRC-approved arrangements or schemes, including the enterprise investment scheme, venture capital scheme or business expansion scheme, able to claim any inheritance tax relief or (except insofar as express reference is made to the treatment of non-UK residents) holding Ordinary Shares in connection with a trade, profession or vocation carried on in the UK (whether through a branch or agency or, in the case of a corporate Shareholder, a permanent establishment or otherwise).*

Prospective investors who are in any doubt as to their tax position or who may be subject to tax in a jurisdiction other than the UK are strongly recommended to consult their own professional advisers.

1. Taxation of dividends

1.1 *UK resident individuals*

An individual Shareholder who is resident for UK tax purposes in the UK will for the 2020/2021 tax year, be entitled to an annual tax-free allowance of £2,000 of dividend income. To the extent that (taking account of any other dividend income received by the Shareholder in the same tax year and excluding dividends paid within an individual savings account or exempt pension arrangement) dividend income exceeds the annual tax free dividend allowance, tax will be imposed at the rates of:

(a) 7.5 per cent, to the extent that the dividend income falls within the basic rate band of income tax;

(b) 32.5 per cent, to the extent that the dividend income falls within the higher rate band of income tax; and

(c) 38.1 per cent, to the extent that the dividend income falls within the additional rate band of income tax.

For the purposes of determining which of the taxable bands dividend income falls into, dividend income is treated as the highest part of a Shareholder's income. In addition, dividends within the nil rate band which (in the absence of the nil rate band exemption) would otherwise have fallen within the basic or higher rate bands will use up those bands respectively and so will be taken into account in determining whether the threshold for higher rate or additional rate income tax is exceeded.

1.2 *Companies*

Shareholders within the charge to UK corporation tax which are "small companies" for the purposes of Chapter 2 of Part 9A of the Corporation Tax Act 2009 will not be subject to UK corporation tax on any dividend received from the Company provided certain conditions are met (including an anti-avoidance condition).

Other Shareholders within the charge to UK corporation tax will not be subject to UK corporation tax on dividends received from the Company so long as the dividends fall within an exempt class and certain

conditions are met. For example, dividends paid on shares that are "ordinary shares" and are not "redeemable" (as those terms are used in Chapter 3 of Part 9A of the Corporation Tax Act 2009), and dividends paid to a person holding less than a 10 per cent interest in the Company, should generally fall within an exempt class. However, the exemptions are not comprehensive and are subject to anti-avoidance rules.

If the conditions for exemption are not met or cease to be satisfied, or such a Shareholder elects for an otherwise exempt dividend to be taxable, the Shareholder will be subject to UK corporation tax on dividends received from the Company.

1.3 *Non-UK resident Shareholders*

An individual Shareholder (other than one carrying on a trade, profession or vocation in the UK) who is not resident for tax purposes in the UK will not generally have any UK tax to pay on cash dividends received from the Company. A company that is not resident for tax purposes in the UK (and that is not otherwise subject to UK tax, e.g. by virtue of carrying on a trade through a UK permanent establishment) will not generally be required to pay UK tax on cash dividends received from the Company.

A Shareholder who is resident outside the UK may be subject to taxation on dividend income under local law. A Shareholder who is not resident solely in the UK for tax purposes or is not subject solely to UK tax on the dividend income (or, in any event, is resident for any tax purpose outside the UK) should consult his (or its) own tax advisers concerning his (or its) tax liabilities (in the UK and any other country) on dividends received from the Company.

1.4 *Withholding taxes*

The Company is not required to withhold UK tax at source from dividend payments it makes to Shareholders.

2. Taxation of disposals

2.1 *General*

A disposal or deemed disposal of Ordinary Shares by a Shareholder who is (at any time in the relevant UK tax year) resident in the UK for tax purposes may give rise to a chargeable gain or an allowable loss for the purposes of UK taxation of capital gains depending upon the Shareholder's circumstances and subject to any available exemption or relief.

The general rule is that, for UK tax purposes, chargeable gains and allowable losses fall to be calculated in sterling. Accordingly, where Ordinary Shares are acquired and/or disposed of for non-sterling consideration, a chargeable gain or allowable loss could arise by reference to exchange rate movements. For Shareholders that are companies within the charge to UK corporation tax, the extent to which this general rule applies may depend on what the company's functional currency is and whether any designated currency election has been made. Prospective investors who are in any doubt as to the consequences for them of these rules should seek appropriate professional advice.

2.2 *UK resident individual Shareholders*

For an individual Shareholder who is (at any time in the relevant UK tax year) resident in the UK for tax purposes, a disposal (or deemed disposal) of Ordinary Shares may give rise to a chargeable gain or an allowable loss for the purposes of capital gains tax. The rate of capital gains tax is generally 10 per cent for individuals who are subject to income tax at the basic rate and 20 per cent for individuals who are subject to income tax at the higher or additional rates. An individual Shareholder is entitled to realise up to a specified amount of gains (£12,300 for tax year 2020/2021) in each tax year without being liable to capital gains tax.

2.3 *UK resident corporate Shareholders*

For a corporate Shareholder within the charge to UK corporation tax, a disposal (or deemed disposal) of Ordinary Shares may give rise to a chargeable gain or an allowable loss for the purposes of UK corporation tax. An indexation allowance on the cost of acquiring the Ordinary Shares may be available to reduce the amount of the chargeable gain which would otherwise arise on the disposal. However, indexation allowance has been removed from 1 January 2018, such that any indexation allowance would be calculated only to 31 December 2017 (and would not apply in respect of Ordinary Shares acquired after 31 December 2017).

2.4 *Non-UK resident Shareholders*

A Shareholder (individual or corporate) who is not resident in the UK for tax purposes is generally not subject to UK capital gains tax. They may, however, be subject to taxation under their local law.

However, if such a Shareholder carries on a trade, profession or vocation in the UK through a branch or agency (or, in the case of a non-UK resident corporate Shareholder, a permanent establishment) to which the Ordinary Shares are attributable, the Shareholder will generally be subject to the same rules that apply to UK resident Shareholders.

An individual Shareholder who acquires Ordinary Shares whilst UK resident and who subsequently ceases to be resident for tax purposes in the UK for a period of (generally) less than five complete years of assessment and who disposes of the Ordinary Shares during that period of non-residence may be liable, on his return to the UK, to capital gains tax in respect of any gain arising from the disposal (subject to any available exemption or relief). Special rules apply to Shareholders who are subject to tax on a "split year" basis, who should seek specific professional advice if they are in any doubt about their position.

3. Inheritance tax

The Ordinary Shares may be assets situated in the UK for the purposes of UK inheritance tax. A gift of such assets by an individual Shareholder, or the death of an individual Shareholder, may therefore give rise to a liability to UK inheritance tax, whether or not the Shareholder is resident or domiciled in the UK, depending upon the Shareholder's circumstances and subject to any available exemption or relief. A transfer of Ordinary Shares at less than market value may be treated for inheritance tax purposes as a gift of the Ordinary Shares. Special rules apply to close companies and to trustees of certain settlements who hold Ordinary Shares, which rules may bring them within the charge to inheritance tax. The inheritance tax rules are complex and Shareholders should consult an appropriate professional adviser in any case where those rules may be relevant, particularly in (but not limited to) cases where Shareholders intend to make a gift of Ordinary Shares, to transfer Ordinary Shares at less than market value or to hold Ordinary Shares through a company or trust arrangement.

4. Stamp Duty and Stamp Duty Reserve Tax

4.1 *General*

The following statements are intended as a general guide to the current UK stamp duty and stamp duty reserve tax ("**SDRT**") position for holders of Ordinary Shares. Certain categories of person, including intermediaries, brokers, dealers and persons connected with depositary receipt systems and clearance services may not be liable to stamp duty or SDRT or may be liable at a higher rate or may, although not primarily liable for tax, be required to notify and account for it under the Stamp Duty Reserve Tax Regulations 1986. The comments in this section relating to stamp duty and SDRT apply whether or not a Shareholder is resident in the UK.

4.2 *Depositary receipt systems and clearance services*

The Company expects that, on Admission, the New Ordinary Shares will be eligible to be held within Euroclear Belgium, the Belgian central securities depository. Under current UK domestic legislation, where UK shares are issued to or transferred to (or to a nominee for) a person whose business is or includes the provision of clearance services for such shares (such as Euroclear Belgium) SDRT or stamp duty may be payable at 1.5% of the amount or value of the consideration payable or, in certain circumstances, the value of the shares or (in a case where the securities are issued) the issue price of such shares. Following litigation, HMRC has confirmed in its published guidance that it will no longer seek to impose the 1.5% SDRT charge on *issuances* of UK shares to clearance services anywhere in the world, on the basis that such a charge is not compatible with EU law. As regards *transfers* of shares to a clearance service, the Court of Justice of the European Union has confirmed, including recently in the case of *Air Berlin v Commissioners for HM Revenue & Customs*, that the imposition of the 1.5% charge on a transfer of shares to a clearance service, where that transfer forms an integral part of an overall transaction with regard to the raising of capital, is also incompatible with European law.

4.3 *Transfers of Ordinary Shares*

While Ordinary Shares are held within the Euroclear Belgium clearance system, provided that Euroclear Belgium satisfies various conditions specified in UK legislation and has not elected and does not elect for a different treatment, electronic book-entry transfers of such shares should not be subject to UK stamp duty or SDRT.

Transfers of, or agreements to transfer, Ordinary Shares from the Euroclear Belgium clearance system into another clearance system should not generally be subject to UK stamp duty or SDRT, provided the clearance systems meet various conditions under UK legislation. However appropriate professional advice should be sought should these circumstances arise or be contemplated.

In the event that Ordinary Shares have left the Euroclear Belgium clearance system, any subsequent transfer or agreement to transfer such shares may be subject to UK stamp duty or SDRT at a rate of 0.5%. If, having left the Euroclear Belgium clearance system, Ordinary Shares are to be transferred back into the Euroclear Belgium system or into another clearance system or depository receipt system, this could give rise to a stamp duty or SDRT charge at the rate of 1.5% of the consideration for such transfer (or, in certain circumstances, 1.5% of the value of such shares).

Prospective investors who are in any doubt as to the stamp duty or SDRT consequences for them of transactions relating to Ordinary Shares should seek appropriate professional advice.

B. CERTAIN US FEDERAL INCOME TAX CONSIDERATIONS

The following is a summary of certain US federal income tax consequences of the acquisition, ownership and disposition of New Ordinary Shares by a US Holder (as defined below). This summary deals only with initial purchasers of New Ordinary Shares that are US Holders and that will hold the New Ordinary Shares as capital assets. The discussion does not cover all aspects of US federal income taxation that may be relevant to, or the actual tax effect that any of the matters described herein will have on, the acquisition, ownership or disposition of New Ordinary Shares by particular investors (including consequences under the alternative minimum tax or net investment income tax), and does not address state, local, non-US or other tax laws. This summary also does not address tax considerations applicable to investors that own (directly, indirectly or by attribution) 10 per cent or more of the stock of the Company (by vote or value), nor does this summary discuss all of the tax considerations that may be relevant to certain types of investors subject to special treatment under the US federal income tax laws (such as financial institutions, insurance companies, individual retirement accounts and other tax-deferred accounts, tax-exempt organisations, dealers in securities or currencies, investors that will hold the New Ordinary Shares as part of straddles, hedging transactions or conversion transactions for US federal income tax purposes, persons that have ceased to be US citizens or lawful permanent residents of the United States, investors holding the New Ordinary Shares in connection with a trade or business conducted outside of the United States, US citizens or lawful permanent residents living abroad or investors whose functional currency is not the US dollar).

As used herein, the term "**US Holder**" means a beneficial owner of New Ordinary Shares that is, for US federal income tax purposes, (i) an individual citizen or resident of the United States, (ii) a corporation created or organised under the laws of the United States or any State thereof, (iii) an estate the income of which is subject to US federal income tax without regard to its source or (iv) a trust if a court within the United States is able to exercise primary supervision over the administration of the trust and one or more US persons have the authority to control all substantial decisions of the trust, or the trust has validly elected to be treated as a domestic trust for US federal income tax purposes.

The US federal income tax treatment of a partner in an entity or arrangement treated as a partnership for US federal income tax purposes that holds New Ordinary Shares will depend on the status of the partner and the activities of the partnership. Prospective purchasers that are entities or arrangements treated as partnerships for US federal income tax purposes should consult their tax advisers concerning the US federal income tax consequences to them and their partners of the acquisition, ownership and disposition of New Ordinary Shares by the partnership.

There is a significant likelihood that the Company will be a passive foreign investment company (a "**PFIC**") for US federal income tax purposes for its current taxable year and may continue to be so classified in future years. The Company's status as a PFIC will subject US Holders of New Ordinary Shares to adverse US federal income tax consequences. See "Passive Foreign Investment Company Considerations" below.

This summary is based on the tax laws of the United States, including the Internal Revenue Code of 1986, as amended (the "**Code**"), its legislative history, existing and proposed regulations thereunder, published rulings and court decisions, all as of the date hereof and all subject to change at any time, possibly with retroactive effect.

THE SUMMARY OF US FEDERAL INCOME TAX CONSEQUENCES SET OUT BELOW IS FOR GENERAL INFORMATION ONLY. IT IS NOT INTENDED TO BE RELIED UPON BY PURCHASERS FOR THE PURPOSE OF AVOIDING PENALTIES THAT MAY BE IMPOSED UNDER THE US INTERNAL REVENUE CODE. ALL PROSPECTIVE PURCHASERS SHOULD

CONSULT THEIR TAX ADVISERS AS TO THE PARTICULAR TAX CONSEQUENCES TO THEM OF ACQUIRING, OWNING, AND DISPOSING OF THE NEW ORDINARY SHARES, INCLUDING THE APPLICABILITY AND EFFECT OF STATE, LOCAL, NON-US AND OTHER TAX LAWS AND POSSIBLE CHANGES IN TAX LAW.

1. Passive Foreign Investment Company Considerations

A foreign corporation will be a PFIC in any taxable year in which, after taking into account the income and assets of the corporation and certain subsidiaries pursuant to applicable "look-through rules" either (i) at least 75 per cent of its gross income is "passive income" or (ii) at least 50 per cent of the average value of its assets is attributable to assets which produce passive income or are held for the production of passive income. The Company has not, and currently does not, generate operating revenue and further holds a significant amount of assets that generate passive income. Based on the composition of the Company's current operations and financial profile, the Company believes that it was, for US federal income tax purposes, a PFIC for its taxable year ended December 31, 2019, and believes that there is a significant likelihood that it will be classified as a PFIC for its current taxable year and may be so classified in future taxable years. In general, if the Company is classified as a PFIC in any year during which a US Holder holds New Ordinary Shares, the Company will generally continue to be treated as a PFIC with respect to such US Holder in all succeeding years, regardless of whether the Company continues to meet the income or asset tests discussed above. However, a US Holder may be able to make a "deemed sale election" with respect to the Company if it ceases to qualify as a PFIC. As further discussed below, a US Holder that makes a deemed sale election will no longer be treated as holding PFIC stock for periods after the effective date of the election.

If the Company is a PFIC in any year during which a US Holder owns New Ordinary Shares, and the US Holder has not made a mark to market election (as described below), the US Holder generally will be subject to special rules (regardless of whether the Company continues to be a PFIC) with respect to (i) any "excess distribution" (generally, any distributions received by the US Holder on the New Ordinary Shares in a taxable year that are greater than 125 per cent of the average annual distributions received by the US Holder in the three preceding taxable years or, if shorter, the US Holder's holding period for the New Ordinary Shares) and (ii) any gain realised on the sale or other disposition of New Ordinary Shares. Under these rules (a) the excess distribution or gain will be allocated rateably over the US Holder's holding period, (b) the amount allocated to the current taxable year and any taxable year prior to the first taxable year in which the Company is a PFIC will be taxed as ordinary income, and (c) the amount allocated to each of the other taxable years will be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year and an interest charge for the deemed deferral benefit will be imposed with respect to the resulting tax attributable to each such other taxable year.

If the Company ceases to be a PFIC, a US Holder may make an election (a "**deemed sale election**") to be treated for US federal income tax purposes as having sold its New Ordinary Shares on the last day of the last taxable year of the Company during which it was a PFIC. A US Holder that makes a deemed sale election will cease to be treated as owning stock in a PFIC. However, gain recognised by a US Holder as a result of making the deemed sale election will be subject to the rules described above.

Under attribution rules, if the Company were a PFIC for any taxable year and any subsidiary or other entity in which the Company held a direct or indirect equity interest is also a PFIC (a "**Lower-tier PFIC**"), US Holders would be deemed to own their proportionate share of any such Lower-tier PFIC and would be subject to US federal income tax according to the rules described above on (i) certain distributions by the Lower-tier PFIC and (ii) a disposition of equity interests of the Lower-tier PFIC, in each case as if the US Holders held such interests directly, even though the US Holders have not received the proceeds of those distributions or dispositions directly. Prospective purchasers should consult their tax advisers regarding the application of the PFIC regime to Lower-Tier PFICs. Additionally, dividends paid by the Company will not be eligible for the reduced rate of tax applicable to "qualified dividend income".

US Holders can avoid the interest charge by making a mark to market election with respect to the New Ordinary Shares (but not with respect to any Lower tier PFICs), provided that the New Ordinary Shares are "marketable". New Ordinary Shares will be marketable if they are regularly traded on certain US stock exchanges, or on a non-US stock exchange if (i) the non-US exchange is regulated or supervised by a governmental authority of the country in which the exchange is located; (ii) the non-US exchange has trading volume, listing, financial disclosure, surveillance and other requirements designed to prevent

fraudulent and manipulative acts and practices, remove impediments to, and perfect the mechanism of, a free and open, fair and orderly, market, and to protect investors; (iii) the laws of the country in which the exchange is located and the rules of the exchange ensure that these requirements are actually enforced; and (iv) the rules of the exchange effectively promote active trading of listed stocks. While not free from doubt, it is the Company's belief that the Euronext Brussels is likely to be considered a qualified exchange. For these purposes, the New Ordinary Shares will be considered regularly traded during any calendar year during which they are traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. Any trades that have as their principal purpose meeting this requirement will be disregarded.

A US Holder that makes a mark to market election must include in ordinary income for each year an amount equal to the excess, if any, of the fair market value of the New Ordinary Shares at the close of the taxable year over the US Holder's adjusted basis in the New Ordinary Shares. An electing holder may also claim an ordinary loss deduction for the excess, if any, of the US Holder's adjusted basis in the New Ordinary Shares over the fair market value of the New Ordinary Shares at the close of the taxable year, but this deduction is allowable only to the extent of any net mark to market gains for prior years. Gains from an actual sale or other disposition of the New Ordinary Shares will be treated as ordinary income, and any losses incurred on a sale or other disposition of the New Ordinary Shares will be treated as an ordinary loss to the extent of any net mark to market gains for prior years. Once made, the election cannot be revoked without the consent of the IRS unless the New Ordinary Shares cease to be marketable. If the Company is a PFIC for any year in which the US Holder owns the New Ordinary Shares but before a mark to market election is made, the interest charge rules described above will apply to any mark to market gain recognised in the year the election is made.

In some cases, a shareholder of a PFIC can avoid the interest charge and the other adverse PFIC consequences described above by making a "qualified electing fund" ("**QEF**") election to be taxed currently on its share of the PFIC's undistributed income. The Company does not, however, expect to provide to US Holders the information regarding this income that would be necessary in order for a US Holder to make a QEF .election with respect to its New Ordinary Shares.

Each US Holder who owns, or who is treated as owning, PFIC stock during any taxable year in which the Company is classified as a PFIC will be required to file IRS Form 8621. Prospective purchasers should consult their tax advisers regarding the requirement to file IRS Form 8621 and the application of the PFIC regime.

2. Dividends

2.1 *General*

Distributions (other than excess distributions subject to the PFIC rules discussed above) paid by the Company out of current or accumulated earnings and profits (as determined for US federal income tax purposes) generally will be taxable to a US Holder as dividend income, and will not be eligible for the dividends received deduction allowed to corporations. Additionally, dividends paid by the Company to a non-corporate US Holder are not expected to be eligible for the special reduced rate of tax applicable to "qualified dividend income". Distributions in excess of current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of the US Holder's basis in the New Ordinary Shares and thereafter as capital gain. However, the Company does not maintain calculations of its earnings and profits in accordance with US federal income tax accounting principles. US Holders should therefore assume that any distribution by the Company with respect to New Ordinary Shares will be reported as ordinary dividend income. US Holders should consult their own tax advisers with respect to the appropriate US federal income tax treatment of any distribution received from the Company. Prospective purchasers should consult their tax advisers concerning the applicability of the foreign tax credit and source of income rules to dividends on the New Ordinary Shares.

2.2 *Foreign Currency Dividends*

Dividends paid in euros generally will be included in income in a US dollar amount calculated by reference to the exchange rate in effect on the day the dividends are received by the US Holder, regardless of whether the euros are converted into US dollars at that time. If dividends received in euros are converted into US dollars on the day they are received, the US Holder generally will not be required to recognise foreign currency gain or loss in respect of the dividend income.

3. Sale or other Disposition

Subject to the PFIC rules discussed above, upon a sale or other disposition of New Ordinary Shares, a US Holder generally will recognise gain or loss for US federal income tax purposes equal to the difference, if any, between the amount realised on the sale or other disposition and the US Holder's adjusted tax basis in the New Ordinary Shares. A US Holder may realise gain on New Ordinary Shares not only through a sale or other disposition, but also by pledging the New Ordinary Shares as security for a loan or entering into certain constructive disposition transactions with respect to the New Ordinary Shares. Any gain realised will be subject to the PFIC rules discussed above. Except for losses allowed as a deduction from ordinary income pursuant to the mark to market rules discussed above, any loss will be a capital loss, and will be a long-term capital loss if the US Holder's holding period in the New Ordinary Shares exceeds one year. Any gain or loss generally will be US source.

A US Holder's tax basis in an New Ordinary Share generally will be its US dollar cost, increased by any amounts included in income under the mark to market rules and rules applicable to Lower-Tier PFICs, and decreased by any amounts deducted from income pursuant to the mark to market rules. The US dollar cost of an New Ordinary Share purchased with foreign currency will generally be the US dollar value of the purchase price on the date of purchase, or the settlement date for the purchase, in the case of New Ordinary Shares traded on an established securities market, within the meaning of the applicable Treasury Regulations, that are purchased by a cash basis US Holder (or an accrual basis US Holder that so elects). Such an election by an accrual basis US Holder must be applied consistently from year to year and cannot be revoked without the consent of the IRS.

The amount realised on a sale or other taxable disposition of New Ordinary Shares for an amount in foreign currency generally will be the US dollar value of such amount on the settlement date of such sale or other taxable disposition in the case of a cash basis US Holder, or the trade date in the case of an accrual basis US Holder. On the settlement date, an accrual basis US Holder generally will recognise US source foreign currency gain or loss (taxable as ordinary income or loss) equal to any difference between the US dollar value of the amount received based on the exchange rates in effect on the trade date and the settlement date. However, in the case of New Ordinary Shares traded on an established securities market, accrual basis US Holders may elect to determine the US dollar value of the amount realised on the sale or other taxable disposition of the New Ordinary Shares based on the exchange rate in effect on the settlement date, and no exchange gain or loss will be recognised on such date.

4. Backup Withholding and Information Reporting

Payments from the proceeds of sale or other disposition of New Ordinary Shares, as well as dividends and other proceeds with respect to New Ordinary Shares, by a US paying agent or other US intermediary will be reported to the IRS and to the US Holder as may be required under applicable regulations. Backup withholding may apply to these payments if the US Holder fails to provide an accurate taxpayer identification number or certification of exempt status or fails to comply with applicable certification requirements. Certain US Holders are not subject to backup withholding. US Holders should consult their tax advisers about these rules and any other reporting obligations that may apply to the ownership or disposition of New Ordinary Shares, including requirements related to the holding of certain foreign financial assets.

C. BELGIAN TAXATION

The paragraphs below present a summary of certain material Belgian federal income tax consequences of the ownership and disposal of the Ordinary Shares by an investor that purchases such New Ordinary Shares in connection with this Fundraising. The summary is based on laws, treaties and regulatory interpretations in effect in Belgium on the date of this Prospectus, all of which are subject to change, including changes that could have retroactive effect.

Investors should appreciate that, as a result of evolutions in law or practice, the eventual tax consequences may be different from what is stated below.

This summary does not purport to address all tax consequences of the ownership and disposal of New Ordinary Shares, and does not take into account the specific circumstances of particular investors, some of which may be subject to special rules, or the tax laws of any country other than Belgium. This summary does not describe the tax treatment of investors that are subject to special rules, such as banks, insurance companies, collective investment undertakings, dealers in securities or currencies, persons that hold, or will hold, the Ordinary Shares as a position in a straddle, share-repurchase transaction, conversion transactions,

synthetic security or other integrated financial transactions. This summary does not address the tax regime applicable to the Ordinary held by Belgian tax residents through a fixed basis or a permanent establishment situated outside Belgium. This summary does not address the local taxes that may be due in connection with an investment in the Ordinary Shares, other than Belgian local surcharges which generally vary from 0 per cent to 9 per cent of the investor's income tax liability.

For purposes of this summary, a Belgian resident is an individual subject to Belgian personal income tax (that is, an individual who is domiciled in Belgium or has his seat of wealth in Belgium or a person assimilated to a resident for purposes of Belgian tax law), a company subject to the ordinary Belgian corporate income tax (that is, a corporate entity that has its statutory seat, its main establishment, its administrative seat or seat of management in Belgium), an Organization for Financing Pensions subject to Belgian corporate income tax (i.e., a Belgian pension fund incorporated under the form of an Organization for Financing Pensions), or a legal entity subject to Belgian income tax on legal entities (that is, a legal entity other than a company subject to Belgian corporate income tax, that has its statutory seat, its main establishment, its administrative seat or seat of management in Belgium). A Belgian non-resident is any person that is not a Belgian resident. Investors should consult their own advisors regarding the tax consequences of an investment in the New Ordinary Shares in the light of their particular circumstances, including the effect of any state, local or other national laws.

1. Dividends

For Belgian income tax purposes, the gross amount of all benefits paid on or attributed to the Ordinary Shares is generally treated as a dividend distribution. By way of exception, the repayment of capital of the Company carried out in accordance with the applicable provisions of Belgian Code of Companies and Associations, is not treated as a dividend distribution to the extent that such repayment is imputed to the fiscal capital. This fiscal capital includes, in principle, the actual paid-up statutory share capital and, subject to certain conditions, the paid-up issuance premiums. Note that as of 2018 (i.e. financial years starting on or after 1 January 2018), any reduction of fiscal capital is deemed to be paid out on a *pro rata* basis of the fiscal capital and certain reserves (i.e. and in the following order: the taxed reserves incorporated in the statutory capital, the taxed reserves not incorporated in the statutory capital and the tax-exempt reserves incorporated in the statutory capital). Only the part of the capital reduction that is deemed to be paid out of the fiscal capital may, subject to certain conditions, not be considered as a dividend distribution for Belgian tax purposes.

A Belgian withholding tax of 30 per cent is normally levied on dividends, subject to such relief as may be available under applicable domestic or double tax treaty provisions.

In the case of a redemption of the Ordinary Shares, the redemption distribution (after deduction of the part of the fiscal capital represented by the redeemed Ordinary Shares) will be treated as a dividend subject to a Belgian withholding tax of 30 per cent, subject to such relief as may be available under applicable domestic or double tax treaty provisions. No Belgian withholding tax will be triggered if this redemption is carried out on Euronext or a similar stock exchange and meets certain conditions.

In case of liquidation of the Company, any amounts distributed in excess of the fiscal capital will in principle be subject to a 30 per cent withholding tax, subject to such relief as may be available under applicable domestic or double tax treaty provisions.

Non-Belgian dividend withholding tax, if any, will neither be creditable against any Belgian income tax due nor reimbursable to the extent that it exceeds Belgian income tax due. In that respect, please note that no UK dividend withholding tax will in principle be applicable on dividend distributions made by the Company (see Section A of this Part XIII (*Taxation*)).

1.1 *Belgian resident individuals*

For Belgian resident individuals who acquire and hold the New Ordinary Shares as a private investment, the Belgian dividend withholding tax fully discharges their personal income tax liability. They may nevertheless opt to report the dividends in their personal income tax return Belgian resident individuals who report the dividends in their personal income tax return will normally be taxable at the lower of the generally applicable 30% Belgian withholding tax rate on dividends or at the progressive personal income tax rates applicable to their overall declared income. If the beneficiary reports the dividends, any income tax due on such dividends will not be increased by communal surcharges. In addition, if the dividends are reported, the Belgian dividend withholding tax levied at source may, in both cases, be credited against the personal income tax due and is reimbursable to the extent that it exceeds the personal income tax due, provided that

the dividend distribution does not result in a reduction in value of or a capital loss on the Ordinary Shares of the Company. The latter condition is not applicable if the individual can demonstrate that it has held the Ordinary Shares in full legal ownership for an uninterrupted period of 12 months prior to the payment or attribution of the dividends. Provided the dividends are reported in the personal income tax return, they will in principle be eligible for the newly introduced tax exemption with respect to ordinary dividends up to an amount of €812 (amount applicable for income year 2020) per year (Article 21, first subsection, of the Belgian Income Tax Code 1992 ("**ITC**")). For the avoidance of doubt, all reported dividends (not only dividends distributed on the Ordinary Shares) are taken into account to assess whether said maximum amount is reached.

For Belgian resident individual investors who acquire and hold the New Ordinary Shares for professional purposes, the Belgian withholding tax does not fully discharge their Belgian income tax liability. Dividends received must be reported by the investor and will be taxable at the investor's personal income tax rate increased with communal surcharges. Belgian withholding tax levied may be credited against the personal income tax due and is reimbursable to the extent that it exceeds the income tax due, subject to two conditions: (i) the taxpayer must own the Ordinary Shares in full legal ownership at the time the dividends are paid or attributed and (ii) the dividend distribution may not result in a reduction in value of or a capital loss on the Ordinary Shares. The latter condition is not applicable if the investor can demonstrate that it has held the full legal ownership of the Ordinary Shares for an uninterrupted period of 12 months prior to the payment or attribution of the dividends.

1.2 *Belgian resident companies*

Corporate income tax

For Belgian resident companies, the dividend income (after deduction of any non-Belgian withholding tax but including any Belgian withholding tax) must be declared in the corporate income tax return and will be subject to a corporate income tax rate of 25% as of assessment year 2021 for financial years starting on or after 1 January 2020. Subject to certain conditions, a reduced corporate income tax rate of 20.4% (including the 2% crisis surcharge) and 20% as of 2020 (i.e. for financial years starting on or after 1 January 2020) applies for Small and Medium Sized Enterprises (as defined by Article 1:24, §1 to §6 of the Belgian Companies Code) on the first €100,000 of taxable profits.

Belgian resident companies can under certain conditions deduct 100% of the gross dividend received from their taxable income (the "**Dividend Received Deduction**"), provided that at the time of a dividend payment or attribution: (i) the Belgian resident company holds an amount of the Ordinary Shares representing at least 10% of the share capital of the Company or a participation in the Company with an acquisition value of at least €2,500,000 (it being understood that only one out of the two tests must be satisfied); (ii) the Ordinary Shares of the Company have been or will be held in full ownership for an uninterrupted period of at least one year immediately prior to the payment or attribution of the dividend; and (iii) the conditions relating to the taxation of the underlying distributed income, as described in Article 203 of the Belgian Income Tax Code ("**the Article 203 ITC Taxation Condition**") are met (together, the "**Conditions for the application of the dividend received deduction regime**").

The Conditions for the application of the dividend received deduction regime depend on a factual analysis and for this reason the availability of this regime should be verified upon each dividend distribution.

Any Belgian dividend withholding tax levied at source can be credited against the Belgian corporate income tax due and is reimbursable to the extent it exceeds such corporate income tax, subject to two conditions: (i) the taxpayer must own the Ordinary Shares of the Company in full legal ownership at the time the dividends are paid or attributed and (ii) the dividend distribution does not result in a reduction in value of or a capital loss on the Ordinary Shares of the Company. The latter condition is not applicable: (i) if the taxpayer can demonstrate that it has held the Ordinary Shares in full legal ownership for an uninterrupted period of 12 months immediately prior to the payment or attribution of the dividends or (ii) if, during that period, the Ordinary Shares never belonged to a taxpayer other than a Belgian resident company or a non-resident company that has, in an uninterrupted manner, invested the Ordinary Shares in a Belgian permanent establishment (the "**PE**") in Belgium.

Organisations for financing pensions

For organisations for financing pensions (the "**OFPs**"), i.e., Belgian pension funds incorporated under the form of an OFP ("*organismen voor de financiering van pensioenen*"/ "*organismes de financement de pensions*") within the meaning of Article 8 of the Belgian Law of 27 October 2006, the dividend income is generally tax-exempt.

Although there is no specific exemption from Belgian dividend withholding tax at source for dividends paid or attributed to OFPs, subject to certain limitations, the Belgian dividend withholding tax can be credited against the OFPs' corporate income tax and is reimbursable to the extent it exceeds the corporate income tax due.

Belgian (or foreign) OFPs not holding the Ordinary Shares – which give rise to dividends – for an uninterrupted period of 60 days in full ownership amounts to a rebuttable presumption that the arrangement or series of arrangements ("*rechtshandeling of geheel van rechtshandelingen*"/"*acte juridique ou un ensemble d'actes juridiques*") which are connected to the dividend distributions, are not genuine ("*kunstmatig*"/"*non authentique*"). The withholding tax exemption will in such case not apply and/or any Belgian dividend withholding tax levied at source on the dividends will in such case not be credited against the corporate income tax, unless counterproof is provided by the OFP that the arrangement or series of arrangements are genuine.

Other taxable legal entities

For taxpayers subject to the Belgium income tax on legal entities, the Belgian dividend withholding tax in principle fully discharges their Belgian income tax liability in this respect.

1.3 *Belgian non-resident individuals and companies*

For non-resident individuals and companies, the dividend withholding tax will be the only tax on dividends in Belgium, unless the non-resident holds the Ordinary Shares in connection with a business conducted in Belgium through a fixed base in Belgium or a Belgian PE.

Dividend payments on the Ordinary Shares through a professional intermediary in Belgium will, in principle, be subject to the 30% withholding tax, unless the Shareholder is resident in a country with which Belgium has concluded a double taxation agreement and delivers the requested affidavit. Non-resident investors can also obtain an exemption of Belgian dividend withholding tax if they are the owners or usufructors of the Ordinary Shares and they deliver an affidavit confirming that they have not allocated the Ordinary Shares to business activities in Belgium and that they are non-residents, provided that the dividend is paid through a Belgian credit institution, stock market company or recognised clearing or settlement institution.

If the New Ordinary Shares of the Company are acquired by a non-resident investor in connection with a business in Belgium, the investor must report any dividends received, which are taxable at the applicable Belgian non-resident individual or corporate income tax rate, as appropriate. Any Belgian withholding tax levied at source can be credited against the Belgian non-resident individual or corporate income tax and is reimbursable to the extent it exceeds the income tax due, subject to two conditions: (i) the taxpayer must own the Ordinary Shares of the Company in full legal ownership at the time the dividends are paid or attributed and (ii) the dividend distribution does not result in a reduction in value of or a capital loss on the Ordinary Shares. The latter condition is not applicable if (i) the non-resident individual or the non-resident company can demonstrate that the Ordinary Shares were held in full legal ownership for an uninterrupted period of 12 months immediately prior to the payment or attribution of the dividends or (ii) with regard to non-resident companies only, if, during the said period, the Ordinary Shares have not belonged to a taxpayer other than a resident company or a non-resident company which has, in an uninterrupted manner, invested the Ordinary Shares in a Belgian PE.

Dividends paid or attributed as of 1 January 2020 to Belgian non-resident individuals who do not use the Ordinary Shares in the exercise of a professional activity, may be exempt from Belgian non-resident individual income tax up to the amount of €812 (for income year 2020). Consequently, if Belgian withholding tax has been levied on dividends paid or attributed to the Ordinary Shares, such Belgian non-resident may request in his or her Belgian non-resident income tax return that any Belgian withholding tax levied on dividends up to the amount of €812 (for income year 2020) be credited and, as the case may be, reimbursed. However, if no Belgian non-resident income tax return has to be filed by the Belgian non-resident individual, any Belgian withholding tax levied on dividends up to such an amount could in principle be reclaimed by filing a request thereto addressed to the tax official to be appointed in a Royal Decree. Such a request has to be made at the latest on 31 of December of the calendar year following the calendar year in which the relevant dividend(s) have been received, together with an affidavit confirming the non-resident individual status and certain other formalities which are still to be determined in a Royal Decree. For the avoidance of doubt, all dividends paid or attributed to the Belgian non-resident individual are taken into account to assess whether the maximum amount of €812 (for income year 2020) is reached (and hence not only the amount of dividends paid or attributed on the Ordinary Shares).

Non-resident companies that have invested their Ordinary Shares in the Company in a Belgian establishment can deduct 100% of the gross dividends included in their taxable profits if, at the date dividends are paid or attributed, the Conditions for the application of the Dividend Received Deduction regime are satisfied. Application of the Dividend Received Deduction regime depends, however, on a factual analysis to be made upon each distribution and its availability should be verified upon each distribution.

Please note that the above withholding tax exemption will not be applicable to dividends which are connected to an arrangement or a series of arrangements ("*rechtshandeling of geheel van rechtshandelingen*"/ "*acte juridique ou un ensemble d'actes juridiques*") for which the Belgian tax administration, taking into account all relevant facts and circumstances, has proven, unless evidence to the contrary, that this arrangement or this series of arrangements is not genuine ("*kunstmatig*"/"*non-authentique*") and has been put in place for the main purpose or one of the main purposes of obtaining the dividend received deduction, the above dividend withholding tax exemption or one of the advantages of the Parent-Subsidiary Directive in another EU Member State. An arrangement or a series of arrangements is regarded as not genuine to the extent that they are not put into place for valid commercial reasons which reflect economic reality.

Prospective holders of the New Ordinary Shares should consult their own tax advisers to determine whether they qualify for a reduction in withholding tax upon payment or attribution of dividends, and, if so, to understand the procedural requirements for obtaining a reduced withholding tax upon the payment of dividends or for making claims for reimbursement.

2. Capital gains and losses on the New Ordinary Shares

2.1 *Belgian resident individuals*

In principle, Belgian resident individuals acquiring the New Ordinary Shares of the Company as a private investment should not be subject to Belgian capital gains tax on the disposal of the New Ordinary Shares; capital losses are not tax deductible.

However, capital gains realised by a private individual are taxable at 33% (plus local surcharges) if the capital gain is deemed to be realised outside the scope of the normal management of the individual's private estate. Capital losses are, however, not tax deductible in such event.

Moreover, capital gains realised by Belgian resident individuals on the disposal of the Ordinary Shares, outside the exercise of a professional activity, to a non-resident company (or body constituted in a similar legal form), to a foreign State (or one of its political subdivisions or local authorities) or to a non-resident legal entity, each time established outside the EEA, are in principle taxable at a rate of 16.5% (plus local surcharges) if, at any time during the five years preceding the sale, the Belgian resident individual has owned, directly or indirectly, alone or with his/her spouse or with certain relatives, a substantial shareholding in the Company (i.e. a shareholding of more than 25% in the Company). Capital losses are, however, not tax deductible in such event.

Belgian resident individuals who hold the Ordinary Shares of the Company for professional purposes are taxable at the ordinary progressive personal income tax rates (plus local surcharges) on any capital gains realised upon the disposal of the Ordinary Shares, except for the Ordinary Shares held for more than five years, which are taxable at a separate rate of 10% (capital gains realized in the framework of the cessation of activities under certain circumstances) or 16.5% (other) (both plus local surcharges). Capital losses on the Ordinary Shares incurred by Belgian resident individuals who hold the Ordinary Shares for professional purposes are in principle tax deductible.

Gains realised by Belgian resident individuals upon the redemption of the Ordinary Shares of the Company or upon the liquidation of the Company are generally taxable as a dividend (see above).

2.2 *Belgian resident companies*

Belgian resident companies are not subject to Belgian capital gains taxation on gains realised upon the disposal of the Ordinary Shares of the Company provided that: (i) the Belgian resident company holds the Ordinary Shares representing at least 10% of the share capital of the Company or a participation in the Company with an acquisition value of at least €2,500,000 (it being understood that only one out of the two tests must be satisfied); (ii) the Article 203 ITC Taxation Condition is satisfied and (iii) the Ordinary Shares have been held in full legal ownership for an uninterrupted period of at least one year.

If one or more of the Conditions for the application of the dividend received deduction regime are not met, as of assessment year 2021 (for financial years starting as of 1 January 2020), any capital gain realized

would be taxable at the standard corporate income tax rate of 25.5% (including the 2% crisis surcharge), unless the reduced corporate income tax rate of 20% applies.

Capital gains realized by Belgian resident companies upon the redemption of the Ordinary Shares by the Company or upon the liquidation of the Company will, in principle, be subject to the same taxation regime as dividends (see above).

Capital losses on the Ordinary Shares of the Company incurred by resident companies are as a general rule not tax deductible.

The Ordinary Shares of the Company held in the trading portfolios of qualifying credit institutions, investment enterprises and management companies of collective investment undertakings are subject to a different regime. The capital gains realized by these investors will be subject to corporate income tax at the general rates, and capital losses are tax deductible. Internal transfers to and from the trading portfolio are assimilated to a realisation.

Belgian resident Organizations for financing pensions

OFPs are, in principle, not subject to Belgian capital gains taxation realized upon the disposal of the Ordinary Shares, and capital losses are not tax deductible.

Other taxable legal entities subject to Belgian legal entities tax

Belgian resident legal entities subject to the legal entities income tax are, in principle, not subject to Belgian capital gains taxation on the disposal of the Ordinary Shares.

Capital gains realized by Belgian resident legal entities upon the redemption of the Ordinary Shares or upon the liquidation of the Company will in principle be taxed as dividends.

Capital losses on the Ordinary Shares incurred by Belgian resident legal entities are not tax deductible.

Belgian non-resident individuals

Capital gains realized on the New Ordinary Shares of the Company by a non-resident individual that has not acquired the New Ordinary Shares in connection with a business conducted in Belgium through a fixed base in Belgium or a Belgian PE are in principle not subject to taxation in Belgium, unless the gain is deemed to be realized outside the scope of the normal management of the individual's private estate and the capital gain is obtained or received in Belgium.

Non-resident individuals who do not use the Ordinary Shares for professional purposes and who have their fiscal residence in a country with which Belgium has not concluded a tax treaty or with which Belgium has concluded a tax treaty that confers the authority to tax capital gains on the Ordinary Shares to Belgium, might be subject to tax in Belgium if the capital gains are obtained or received in Belgium and arise from transactions which are to be considered speculative or beyond the normal management of one's private estate or in the event of disposal of a substantial participation in a Belgian company as mentioned in the tax treatment of the disposal of the Ordinary Shares by Belgian individuals (see section C.2.1 here above).

Capital gains realized by Belgian non-resident individuals upon the redemption of the Ordinary Shares or upon the liquidation of the Company will generally be taxable as a dividend (see above).

Belgian non-resident companies or entities

Capital gains realized by non-resident companies or other non-resident entities that hold the New Ordinary Shares in connection with a business conducted in Belgium through a Belgian PE are generally subject to the same regime as Belgian resident companies.

2.3 ***Tax on stock exchange transactions***

No tax on stock exchange transactions is due upon subscription to the Ordinary Shares (primary market transactions).

The purchase and the sale and any other acquisition or transfer for consideration of existing Ordinary Shares (secondary market transactions) is subject to the tax on stock exchange transactions (*taks op de beursverrichtingen/taxe sur les opérations de bourse*) of 0.35%. of the purchase price, capped at €1,600 per transaction and per party if (i) it is entered into or carried out in Belgium through a professional intermediary or (ii) deemed to be entered into or carried out in Belgium, which is the case if the order is directly or indirectly made to a professional intermediary established outside of Belgium, either by private

individuals with habitual residence in Belgium, or legal entities for the account of their seat or establishment in Belgium (both referred to as a "**Belgian Investor**").

Following the Law of 25 December 2016, the scope of application of the tax on the stock exchange transactions has been extended as of 1 January 2017 to secondary market transactions of which the order is, directly or indirectly, made to a professional intermediary established outside of Belgium by a Belgian Investor. In such a scenario, the tax on the stock exchange transactions is due by the Belgian Investor, unless the Belgian Investor can demonstrate that the tax on the stock exchange transactions due has already been paid by the professional intermediary established outside of Belgium. In the latter case, the foreign professional intermediary also has to provide each client (which gives such intermediary an order) with a qualifying order statement (bordereau/borderel), at the latest on the business day after the day the transaction concerned was realised. Alternatively, professional intermediaries established outside of Belgium could appoint a stock exchange tax representative in Belgium, subject to certain conditions and formalities ("**Stock Exchange Tax Representative**"). Such Stock Exchange Tax Representative will then be liable towards the Belgian Treasury for the tax on stock exchange transactions due and for complying with reporting obligations and the obligations relating to the order statement in that respect. If such a Stock Exchange Tax Representative would have paid the tax on stock exchange transactions due, the Belgian Investor will, as per the above, no longer be the debtor of the tax on stock exchange transactions.

No tax on stock exchange transactions is due on transactions entered into by the following parties, provided they are acting for their own account: (i) professional intermediaries described in Article 2, 9° and 10° of the Belgian Law of 2 August 2002 on the supervision of the financial sector and financial services; (ii) insurance companies described in Article 2, § 1 of the Belgian Law of 9 July 1975 on the supervision of insurance companies; (iii) pension institutions referred to in Article 2,1° of the Belgian Law of 27 October 2006 concerning the supervision of pension institutions; (iv) collective investment institutions; (v) regulated real estate companies; and (vi) Belgian non-residents provided they deliver a certificate to their financial intermediary in Belgium confirming their non-resident status.

As stated in Part II (*Risk Factors*), on 14 February 2013 the EU Commission adopted the Draft Directive on a Financial Transaction Tax (the FTT). The Draft Directive currently stipulates that once the FTT enters into effect, the Participating Member States shall not maintain or introduce any taxes on financial transactions other than the FTT (or VAT as provided in the Council Directive 2006/112/EC of 28 November 2006 on the common system of value added tax). For Belgium, the tax on stock exchange transactions should thus be abolished once the FTT enters into effect. The Draft Directive is still subject to negotiation between the Participating Member States and may, therefore, be further amended at any time.

3. Common reporting standard

Following recent international developments, the exchange of information will be governed by the Common Reporting Standard ("**CRS**"). More than 100 jurisdictions signed the multilateral competent authority agreement ("**MCAA**"), which is a multilateral framework agreement to automatically exchange financial and personal information, with the subsequent bilateral exchanges coming into effect between those signatories that file the subsequent notifications. Under CRS, financial institutions resident in a CRS country will be required to report, according to a due diligence standard, financial information with respect to reportable accounts, which includes interest, dividends, account balance or value, income from certain insurance products, sales proceeds from financial assets and other income generated with respect to assets held in the account or payments made with respect to the account. Reportable accounts include accounts held by individuals and entities (which includes trusts and foundations) with fiscal residence in another CRS country. The standard includes a requirement to look through passive entities to report on the relevant controlling persons.

On 9 December 2014, EU Member States adopted Directive 2014/107/EU on administrative cooperation in direct taxation ("**DAC2**"), which provides for mandatory automatic exchange of financial information as foreseen in CRS. DAC2 amends the previous Directive on administrative cooperation in direct taxation, Directive 2011/16/EU.

The mandatory automatic exchange of financial information by EU Member States as foreseen in DAC2 takes place as of 30 September 2017 at the latest, except with regard to Austria. The mandatory automatic exchange of financial information by Austria will at the latest take place as of 30 September 2018.

The Belgian government has implemented said Directive 2014/107/EU, respectively the Common Reporting Standard, per the Law of 16 December 2015 regarding the exchange of information on financial accounts by

Belgian financial institutions and by the Belgian tax administration, in the context of an automatic exchange of information on an international level and for tax purposes.

As a result of the Law of 16 December 2015, the mandatory automatic exchange of information applies in Belgium (i) as of income year 2016 (first information exchange in 2017) towards the EU Member States (including Austria, irrespective the fact that the automatic exchange of information by Austria towards other EU Member States is only foreseen as of income year 2017), (ii) as of income year 2014 (first information exchange in 2016) towards the US and (iii), with respect to any other non-EU States that have signed the MCAA, as of the respective date to be further determined by Royal Decree.

Investors who are in any doubt as to their position should consult their professional advisers.

PART XIV

ADDITIONAL INFORMATION

1. Responsibility statement

The Company and the Directors, whose names appear on page 39 of this document, accept responsibility for the information contained in this document. To the best of the knowledge of the Company and the Directors, the information contained in this document is in accordance with the facts and this document makes no omission likely to affect its import.

2. Incorporation and activity of the Company

2.1 The Company was incorporated and registered in England and Wales under the Companies Act as a private company limited by shares on 2 September 2015 under the name Cityviva Limited, with registered number 9759376. On 22 September 2015, the Company was registered as a public company limited by shares and changed its name to Acacia Pharma Group plc. On 19 December 2016, the Company was registered as a private company limited by shares and changed its name to Acacia Pharma Group Limited. On 21 February 2018, the Company was registered as a public company limited by shares and changed its name to Acacia Pharma Group plc.

2.2 The Ordinary Shares have been admitted to trading on the regulated market of Euronext Brussels since 6 March 2018.

2.3 The Company is domiciled in the UK. Its registered office and head office is at The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH (telephone number: 01223 919760). The Company's website is www.acaciapharma.com. The Company's LEI code is 213800SLDKXWKT6E3381.

2.4 The principal legislation under which the Company operates, and under which the New Ordinary Shares will be created, is the Companies Act and regulations made thereunder. The Company operates in conformity with its constitution.

2.5 The Company became the holding company of the Group on 14 September 2015.

3. Share capital

3.1 The ISIN of the Ordinary Shares is GB00BYWF9Y76. The Company's LEI code is 213800SLDKXWKT6E3381.

3.2 As at the Latest Practicable Date, the Company had 72,779,729 Ordinary Shares in issue and no Ordinary Shares were held in treasury. No Ordinary Shares have been issued other than fully paid.

3.3 Pursuant to a loan agreement dated 23 February 2016 which has been terminated, the Company issued warrants over 127,500 shares of £0.02 each to Silicon Valley Bank and Life Sciences Loans, LLC exercisable at £4 per share. The warrants are currently outstanding and have not been exercised.

3.4 As at the Latest Practicable Date, and save as otherwise disclosed in Sections 3, 9, 10, 18.5, 18.9 and 18.11 of this Part XIV (*Additional Information*):

(a) the Company has not issued any convertible securities, exchangeable securities or securities with warrants; and

(b) the Company has not granted or assumed any acquisition rights or obligations over unauthorised but unissued share capital or given any undertaking to increase the share capital.

3.5 Pursuant to resolutions of the Company dated 7 April 2020, the Directors were generally and unconditionally authorised pursuant to section 551 of the Companies Act (in addition to any existing authority pursuant to such section) to exercise all of the powers of the Company to allot Ordinary Shares up to an aggregate nominal amount of £640,000.00 in connection with future offerings of Ordinary Shares for cash pursuant to sections 570 to 573 of the Companies Act and to sell Ordinary Shares from treasury as if section 561 of the Companies Act did not apply to such allotment or sale, such authorities to expire at the next annual general meeting of the Company save that the Company may, before the expiry of the authority, enter into an agreement which would or might require Ordinary Shares to be allotted or sold from treasury after the expiry of such power, and the Directors may allot Ordinary Shares or sell Ordinary Shares from treasury in pursuance of such an offer or agreement as if such power had not expired.

3.6 The New Ordinary Shares will carry the right to receive dividends and distributions paid by the Company following their Admission. All Shareholders will have the right to receive notice of and to attend and vote at all general meetings of the Company.

4. Information about the Ordinary Shares

4.1 *Description of the type and class of securities being offered*

The New Ordinary Shares being offered pursuant to the Fundraising have a nominal value of £0.02 each. Upon their Admission the Company will continue to have one class of issued shares (Ordinary Shares), the rights of which are set out in the Articles, a summary of which is set out in Section 5 of this Part XIV (*Additional Information*).

Each of the New Ordinary Shares offered pursuant to the Fundraising will be credited as fully paid and free from all liens, equities, charges, encumbrances and other interests.

The Existing Ordinary Shares and the New Ordinary Shares (when issued and fully paid) will rank equally in all respects with each other, including in full for all dividends and distributions on Ordinary Shares declared, made or paid after their issue and in relation to voting rights and rights on a return of capital, as set out in the Articles.

4.2 *Legislation under which the Ordinary Shares are created*

The Ordinary Shares have been, and the New Ordinary Shares will be, created under the Companies Act and they will conform with the laws of England and Wales. The Ordinary Shares have been and will be duly authorised according to the requirements of the Company's constitution and have and will have all necessary statutory and other consents.

4.3 *Form and currency of the Ordinary Shares*

The form of subscription and method of entry of the Ordinary Shares are governed by the laws of England and Wales, which requires that the shares are subscribed and registered in the share register of the Company held by Equiniti Limited of Aspect House, Spencer Road, Lancing, West Sussex BN99 6DA.

All New Ordinary Shares will be delivered in book-entry form only, and will be credited to the relevant securities accounts via Euroclear Belgium, the central securities depository, Koning Albert II laan 1, B-1210 Brussels, Belgium. The New Ordinary Shares will be registered in the name of Euroclear Belgium in the register of the Company.

Title to certificated New Ordinary Shares (if any) will be evidenced by entry in the register of members of the Company and title to uncertificated New Ordinary Shares will be evidenced by entry in the operator register maintained by Euroclear Belgium (which forms part of the register of members of the Company).

Investors who, after delivery, wish to have their shares registered, should request that the Company record the New Ordinary Shares in the Company's share register.

No share certificates will be issued in respect of New Ordinary Shares held in uncertificated form. If any such New Ordinary Shares are converted to be held in certificated form, share certificates will be issued in respect of those New Ordinary Shares in accordance with applicable legislation. No temporary documents of title have been or will be issued in respect of the New Ordinary Shares.

The Ordinary Shares are denominated in pounds sterling.

4.4 *Rights attaching to the Ordinary Shares*

Subject to the provisions of the Companies Act, any equity securities issued by the Company for cash must first be offered to Shareholders in proportion to their holdings of Ordinary Shares. The Companies Act allows for the disapplication of pre-emption rights which may be waived by a special resolution of the Shareholders, either generally or specifically, for a maximum period not exceeding five years. Please see Section 3 of this Part XIV (*Additional Information*) for a description of the waivers of pre-emption rights that have applied since completion of the IPO.

Except in relation to dividends which have been declared and rights on a liquidation of the Company, the Shareholders have no rights to share in the profits of the Company.

The Ordinary Shares are not redeemable. However, the Company may purchase or contract to purchase any of the Ordinary Shares on or off-market, subject to the Companies Act. The Company may purchase

Ordinary Shares only out of distributable reserves or the proceeds of a new issue of shares made for the purpose of funding the repurchase.

Further details of the rights attaching to the Ordinary Shares in relation to attendance and voting at general meetings, dividend rights, entitlements on a winding-up of the Company and transferability of shares are set out in Section 5 of this Part XIV (*Additional Information*).

4.5 *Description of restrictions on free transferability of the New Ordinary Shares*

Save as described below, the New Ordinary Shares will be freely transferable upon their Admission.

Transfer of shares under the Articles

Subject to the provisions of the Companies Act, the Board may, in its absolute discretion, decline to register any transfer of any share which is not a fully paid share provided that where such a share is a member of a class of share admitted to the regulated market of Euronext Brussels, such discretion may not be exercised in such a way as to prevent dealings in shares of that class from taking place on an open and proper basis. The Board may also decline to register a transfer of a certificated share unless the instrument of transfer:

(a) is left at the registered office of the Company or such other place as the Board may from time to time determine accompanied (save in the case of a transfer by a person to whom the Company is not required by law to issue a certificate and to whom a certificate has not been issued) by the certificate for the share to which it relates and such other evidence as the Board may reasonably require to show the right of the person executing the instrument of transfer to make the transfer;

(b) (if stamp duty is generally chargeable on transfers of certificated shares) is duly stamped or certified or otherwise shown to the satisfaction of the Board to be exempt from stamp duty and is accompanied by the relevant share certificate or such other evidence of the right to transfer as the Board may reasonably require;

(c) is in respect of only one class of share; and

(d) if to joint transferees, is in favour of not more than four such transferees.

Registration of a transfer of an uncertificated share may only be refused in the circumstances set out in the rules and procedures of Euroclear Belgium and where, in the case of a transfer to joint holders, the number of joint holders to whom the uncertificated share is to be transferred exceeds four.

The Board may decline to register a transfer of any of the Company's certificated shares by a person with any interest (as defined in the Articles) if such a person has been served with a restriction notice (as defined in the Articles) after failure to provide the Company with information concerning interests in those shares required to be provided under the Companies Act, unless the transfer is shown to the Board to be pursuant to an arm's length sale (as defined in the Articles).

Transfer restrictions under the Companies Act

The Company may, under the Companies Act, send out statutory notices to those it knows or has reasonable cause to believe have an interest in its shares, asking for details of those who have an interest and the extent of their interest in a particular holding of shares. When a person receives a statutory notice and fails to provide any information required by the notice within the time specified in it, the Company can apply to the court for an order directing, among other things, that any transfer of shares which are the subject of the statutory notice is void.

5. Summary of the Articles

The Articles are available for inspection at the addresses specified in Section 23 of this Part XIV (*Additional Information*). The Articles contain provisions (among others) to the following effect:

5.1 *Limited liability*

The liability of the Company's members is limited to any unpaid amount on the shares in the Company held by them.

5.2 *Voting rights*

(a) Votes on a show of hands

Subject to any special terms as to voting upon which any shares may be issued or may for the time being be held, on a show of hands every Shareholder present in person or by proxy at a general meeting of the

Company and every duly authorised corporate representative shall have one vote. If a proxy has been duly appointed by more than one Shareholder entitled to vote on the resolution and the proxy has been instructed by one or more of those Shareholders to vote for the resolution and by one or more other of those Shareholders to vote against it then the proxy shall have one vote for and one vote against the resolution.

(b) Votes on a poll

Subject to any special terms as to voting upon which any shares may be issued or may for the time being be held and to any other provisions of the Articles or the Companies Act, on a poll every Shareholder present in person or by proxy shall have one vote for every share held by him and every person appointed as proxy of a Shareholder shall have one vote for every share in respect of which he is appointed as a proxy provided always that where a Shareholder appoints more than one proxy, this does not authorise the exercise by such proxies taken together of more extensive voting rights than could be exercised by the Shareholder in person and every duly authorised corporate representative may exercise all the powers on behalf of the company which authorised him to act as its representative and shall have one vote for every share in respect of which he is appointed the corporate representative.

5.3 *Dividends and return of capital*

Subject to the provisions of the Companies Act, the Company may by ordinary resolution from time to time declare dividends in accordance with the respective rights of Shareholders, but no dividend shall exceed the amount recommended by the Board.

If the Company shall be wound up (whether the liquidation is voluntary or by the court) the liquidator may, with the authority of a special resolution passed at a general meeting of the Company, divide among the Shareholders in specie or kind the whole or any part of the assets of the Company and whether or not the assets shall consist of property of one kind or shall consist of properties of different kinds, and may for such purposes set such value as he deems fair upon any one or more class or classes of property and may determine how such division shall be carried out as between the Shareholders or different classes of Shareholders. The liquidator may, with the like authority, vest any part of the assets in trustees upon such trusts for the benefit of Shareholders as the liquidator with the like authority shall think fit, and the liquidation of the Company may be closed and the Company dissolved, but so that no Shareholder shall be compelled to accept any shares or other property in respect of which there is a liability.

5.4 *Unclaimed dividends*

If a dividend is left uncashed or is returned to the Company and after reasonable enquiries the Company is unable to establish any new address or a new account, or such a payment is left uncashed or returned to the Company on two separate occasions, the Company is not obliged to send any dividends or other sums payable to that person until he notifies the Company of his new address or new account to be used for that purpose.

5.5 *Transfer of shares*

Any Shareholder may transfer all or any of his uncertificated shares by means of a relevant system in such manner provided for, and subject as provided, in the rules and procedures of Euroclear Belgium and the rules of any relevant system. The Company must maintain a record of uncertificated shares in accordance with the statutes.

Any Shareholder may transfer all or any of his certificated shares by an instrument of transfer in writing in any usual form or in any other form which the Board may approve. The instrument of transfer shall be executed by or on behalf of the transferor and (in the case of a partly paid share) the transferee, and the transferor shall be deemed to remain the holder of the share concerned until the name of the transferee is entered in the register in respect of it. All instruments of transfer, when registered, may be retained by the Company.

Subject to the provisions of the Companies Act, the Board may, in its absolute discretion, decline to register any transfer of any share which is not a fully paid share provided that where such a share is a member of a class of share admitted to the regulated market of Euronext Brussels, such discretion may not be exercised in such a way as to prevent dealings in shares of that class from taking place on an open and proper basis. The Board may also refuse to register any transfer of shares, whether fully paid or not, in favour of more than four persons jointly.

The Board may decline to register any transfer of a certificated share unless:

(a) it is left at the Company's registered office (or such other place as the Board may determine) accompanied by the certificate(s) of the shares to which it relates and such other evidence as the Board may reasonably require to show the right of the transferor to make the transfer; and

(b) the instrument of transfer is in respect of only one class of share.

5.6 *Alteration of share capital*

The Company may exercise the powers conferred by the applicable statutory provisions to:

(a) increase its share capital by allotting new shares;

(b) reduce its share capital, any capital redemption reserve and any share premium account in any way;

(c) sub-divide or consolidate and divide all or any of its share capital;

(d) issue redeemable shares; and

(e) purchase all or any of its own shares including any redeemable shares.

5.7 *Authority to allot shares and grant rights and disapplication of pre-emption rights*

The Company may from time to time pass an ordinary resolution authorising, in accordance with section 551 of the Companies Act, the Board to exercise all the powers of the Company to allot shares or to grant rights to subscribe for or to convert any security into shares in the Company up to the maximum nominal amount specified in the resolution. The authority shall expire on the day specified in the resolution (not being more than five years from the date on which the resolution is passed).

Subject (other than in relation to the sale of treasury shares) to the Board being generally authorised to allot shares and grant rights to subscribe for or to convert any security into shares in the Company in accordance with section 551 of the Companies Act, the Company may from time to time resolve, by special resolution, that the Board be given power to allot equity securities for cash as if section 561(1) of the Companies Act did not apply to the allotment but that power shall be limited to (A) the allotment of equity securities in connection with a rights issue; and (B) the allotment (other than in connection with a rights issue) of equity securities having a nominal amount not exceeding in aggregate the sum specified in the special resolution.

5.8 *Restrictions on shares*

Where the holder of any shares in the Company, or any other person appearing to be interested in those shares, fails to comply within the relevant period (as defined below) with any notice under section 793 of the Companies Act in respect of those shares (in this sub-section, a "statutory notice"), the Company may give the holder of those shares a further notice (in this sub-section, a "restriction notice") to the effect that from the service of the restriction notice the holder of such shares shall not, nor shall any transferee to which any of such shares are transferred, be entitled to be present or to vote on any question, either in person or by proxy, at any general meeting of the Company or separate general meeting of the holders of any class of shares of the Company, or to be counted in a quorum.

If after the service of a restriction notice in respect of any shares the Board is satisfied that all information required by any statutory notice relating to those shares or any of them from their holder or any other person appearing to be interested in the shares the subject of the restriction notice has been supplied, the Company shall, within seven days, cancel the restriction notice. The Company may at any time at its discretion cancel any restriction notice or exclude any shares from it. A restriction notice shall automatically cease to have effect in respect of any shares transferred where the transfer is a "permitted transfer" (as defined below).

The relevant period referred to above is the period of 14 days following service of a statutory notice.

In the case of a restriction notice served on a person having an interest in shares in the Company which comprise in total at least 0.25 per cent in number or nominal value of the shares of the Company (calculated exclusive of any treasury shares), or of any class of such shares, then the restriction notice may also direct that:

(a) the Board may withhold payment of all or any part of any dividends (including shares issued in lieu of dividends) payable in respect of the shares;

(b) where an offer of the right to elect to receive shares of the Company instead of cash in respect of any dividend or part thereof is or has been made by the Company, any election made by a member of the Company who at the time holds restricted shares shall not be effective; and

(c) the Board may (subject to the requirements of the rules and procedures of Euroclear Belgium) decline to register a transfer of the shares unless:

(i) the transfer is a "permitted transfer" (as defined below); or

(ii) the Shareholder is not himself in default as regards the supply of information required and the transfer is only part of the Shareholder's holding and when presented for registration, a certificate is presented in a form satisfactory to the Board to the effect that it is satisfied that none of the shares subject to the transfer are restricted,

and in any other case means only the restriction specified in sub-paragraph (a) above.

A "permitted transfer" referred to above means:

(a) a transfer by way of an acceptance of a takeover for the Company; or

(b) an arm's length transfer of the whole of the beneficial ownership; or

(c) the transfer results from a sale through a recognised investment exchange.

5.9 *Variation of rights attaching to shares*

Subject to the provisions of the Companies Act, all or any of the rights attached to any class of shares for the time being issued may from time to time (whether or not the Company is being wound up) be varied either with the consent in writing of the holders of not less than three-fourths in nominal value of the issued shares of that class (excluding any shares of that class held as treasury shares) or with the sanction of a special resolution passed at a separate general meeting of the holders of those shares.

5.10 *Conditions governing the manner in which annual general meetings and general meetings are called*

The Board shall convene and the Company shall hold general meetings as annual general meetings in accordance with the requirements of the Companies Act. The Board may convene a general meeting whenever it thinks fit.

An annual general meeting shall be convened by not less than 21 clear days' notice in writing. Subject to the Companies Act, all other general meetings shall be convened by not less than 14 clear days' notice in writing.

Notice of every general meeting shall be given to all Shareholders other than any who, under the provisions of the Articles or the terms of issue of the shares they hold, are not entitled to receive such notices from the Company. Notice of every general meeting must also be given to the Company's auditors.

Before a general meeting carries out business, there must be a quorum present. Unless the Articles state otherwise in relation to a particular situation, a quorum for all purposes is two Shareholders present in person or by proxy or by a duly authorised corporate representative and entitled to vote.

5.11 *Notices to Shareholders*

Any notice or document (including a share certificate) may be served on or delivered to any Shareholder by the Company either personally or by sending it through the post addressed to the Shareholder at his registered address or by leaving it at that address addressed to the Shareholder or by means of a relevant system or, where appropriate, by sending it in electronic form to an address for the time being notified by the Shareholder concerned to the Company for that purpose, or by publication on a website in accordance with the Companies Act or by any other means authorised in writing by the Shareholder concerned. In the case of joint holders of a share, service or delivery of any notice or document on or to the joint holder first named in the Register in respect of the share, shall for all purposes be deemed a sufficient service on or delivery to all the joint holders.

5.12 *Directors*

Unless otherwise determined by ordinary resolution of the Company, the number of Directors (disregarding alternate directors) shall not be less than two. The Company may by ordinary resolution vary the minimum and maximum number of the Directors.

Each Director shall retire from office at the third annual general meeting after the annual general meeting at which he was elected or re-elected (as the case may be).

The Company may by ordinary resolution appoint any person who is willing to act to be a Director, either to fill a vacancy or as an addition to the existing Board. Without prejudice to this power the Board may appoint any person who is willing to act to be a Director, either to fill a vacancy or as an addition to the existing Board.

Only the following people can be elected as Directors at a general meeting:

(a) a Director who is retiring at the annual general meeting;

(b) a person who is recommended by the Board; or

(c) a person in respect of who, between seven and 42 days before the date of the meeting, a notice in writing is left at the Company's registered office indicating his willingness to be appointed as well as a notice in writing signed by a Shareholder qualified to vote at the meeting indicating his intention to propose that person for appointment.

The Company may by ordinary resolution of which special notice has been given in accordance with the Companies Act, remove any Director before the expiration of his period of office. The Company may by ordinary resolution, appoint another person in place of such a Director.

The Directors shall be paid out of the funds of the Company by way of fees for their services as directors, such sums (if any) and such benefits in kind as the Board may from time to time determine and such remuneration may either be a fixed sum of money, or may altogether or in part be governed by the business done or profits made, and may include the making of provisions for the payment to him, his widow or other dependants, of a pension on retirement from the office or employment to which he is appointed and for the participation in pension and life assurance and other benefits, or may be upon such other terms as the Directors determine.

Any Director who is appointed to any executive office or who performs services which in the opinion of the Board or any committee authorised by the Board go beyond the ordinary duties of a Director may be paid such extra remuneration (whether by way of salary, percentage of profits or otherwise) as the Board may in its discretion decide.

The Board or any committee authorised by the Board may exercise all the powers of the Company to provide benefits, either by the payment of gratuities or pensions or by insurance or in any other manner whether similar to the foregoing or not, for any director or former director or the relations, connections or dependants of any director or former director of any body corporate which is or was a subsidiary undertaking or a parent undertaking of the Company or another subsidiary undertaking of a parent undertaking, or otherwise associated with the Company or any such body corporate or predecessor in business of the Company or any such body corporate, and to the spouses, civil partners, former spouses, former civil partners, children and other relatives and dependants of any such persons and may establish, maintain, support, subscribe to and contribute to all kinds of schemes, trusts and funds (whether contributory or non-contributory) for the benefit of such persons as referred to above.

Save as otherwise provided in the Articles, a Director shall not vote on, or be counted in the quorum in relation to, any resolution of the Board in respect of any actual or proposed transaction or arrangement with the Company in which he has an interest which may reasonably be regarded as likely to give a rise to a conflict of interest otherwise than by virtue of interests in shares or other securities in or through Company. This prohibition shall not apply to any resolution where that material interest arises only from one or more of the following matters:

(a) the giving to him of any guarantee, indemnity or security in respect of money lent or obligations undertaken by him or by any other person at the request of or for the benefit of the Company or any of its subsidiary undertakings;

(b) the giving to a third party of any guarantee, indemnity or security in respect of a debt or obligation of the Company or any of its subsidiary undertakings for which he himself has assumed responsibility in whole or in part under a guarantee or indemnity or by the giving of security;

(c) where the Company or any of its subsidiary undertakings is offering securities in which offer the Director is or may be entitled to participate as a holder of securities or in the underwriting or sub-underwriting of which the Director is to participate;

(d) any contract in which he is interested by virtue of his interest in shares or debentures or other securities of the Company or by reason of any other interest in or through the Company;

(e) any contract for the benefit of the employees of the Company or of any of its subsidiary undertakings under which he benefits in a similar manner to the employees and which does not accord to any Director as such any privilege or advantage not accorded to the employees to whom the contract relates;

(f) any contract concerning any insurance which the Company is to purchase and maintain for the benefit of Directors;

(g) the giving of an indemnity pursuant to the Articles (see Section 5.13, below); and

(h) the provision of funds to any Director to meet or prevent from incurring expenditure under section 205(1) or 206 of the Companies Act.

If any question arises at any meeting of the Board as to whether the interest of a Director gives rise to a conflict, or could reasonably be regarded as likely to give rise to a conflict, with the interests of the Company or as to the entitlement of any Director to vote or be counted in the quorum and the question is not resolved by him voluntarily agreeing to abstain from voting or not to be counted in the quorum, the question shall be referred to the chairman of the meeting and his ruling shall be final and conclusive except in a case where the nature or extent of the interest of the Director concerned has not been fairly disclosed.

The Directors may authorise any matter proposed to them in accordance with the Articles which would, if not so authorised, constitute or give rise to an infringement of duty by a Director under section 175 of the Companies Act. Such authorisation shall only be effective if:

(a) the matter in question was proposed by any person for consideration at a meeting of the Directors and such matter was subsequently considered by the Directors;

(b) any requirement as to the quorum at the meeting of the Directors at which the matter is considered is met without counting the Director in question and any other interested Director; and

(c) the matter was agreed to without such interested Director or Directors voting or would have been agreed to if the votes of such interested Director or Directors had not been counted.

5.13 *Indemnity of Directors*

To the extent permitted by the Companies Act, the Company may indemnify any director or former director of the Company or of any associated company against any liability and may purchase and maintain for any director or former director of the Company or of any associated company insurance against any liability.

5.14 *Borrowing powers*

Subject to the provisions of the Companies Act, the Board may exercise all the powers of the Company to borrow money, and to mortgage or charge its undertaking, property and assets (present and future) and uncalled capital, or any part thereof, and subject to the provisions of the statutes to issue debentures and other securities, whether outright or as collateral security for any debt, liability or obligation of the Company or of any third party.

The Board shall restrict the borrowings of the Company and exercise all voting and other rights or powers of control exercisable by the Company in relation to its subsidiaries so as to secure that the aggregate amount for the time being remaining undischarged of all moneys borrowed by the Group (exclusive of borrowings owing by one member of the Group to another member of the Group) shall not at any time without the previous sanction of an ordinary resolution of the Company exceed an amount equal to the higher of (i) £40 million and (ii) two times the aggregate from time to time of the amount paid up on the issued share capital of the Company and the Company's adjusted capital and reserves (as defined in the Articles).

6. Mandatory bids and compulsory acquisition rules relating to the Ordinary Shares

Other than as provided by the City Code and Part 28 of the Companies Act, there are no rules or provisions relating to mandatory bids and/or squeeze-out and sell-out rules that apply to the Ordinary Shares or the Company.

6.1 *Mandatory bids*

Given that the shared jurisdiction rules under the Takeover Directive apply to the Company, mandatory public takeover bids are triggered under Rule 9 of the City Code. Under Rule 9 of the City Code, if an acquisition of interests in shares were to increase the aggregate holding of the acquirer and its concert parties to interests in shares carrying 30 per cent or more of the voting rights in the Company, the acquirer and, depending on the circumstances, its concert parties would be required (except with the consent of the Takeover Panel) to make a cash offer for the outstanding shares in the Company at a price not less than the highest price paid for interests in shares by the acquirer or its concert parties during the previous 12 months. This requirement would also be triggered by any acquisition of interests in shares by a person holding (together with its concert parties) shares carrying between 30 per cent and 50 per cent of the voting rights in the Company if the effect of such acquisition were to increase that person's percentage of the total voting rights in the Company.

"Interests in shares" is defined broadly in the City Code. A person who has long economic exposure, whether absolute or conditional, to changes in the price of shares will be treated as interested in those shares. A person who only has a short position in shares will not be treated as interested in those shares.

"Voting rights" for these purposes means all the voting rights attributable to the share capital of a company which are currently exercisable at a general meeting.

Persons acting in concert (and concert parties) comprise persons who, pursuant to an agreement or understanding (whether formal or informal), co-operate to obtain or consolidate control of a company or to frustrate the successful outcome of an offer for a company. Certain categories of people are deemed under the City Code to be acting in concert with each other unless the contrary is established.

6.2 *Squeeze-out rules*

Under the Companies Act, if a "takeover offer" (as defined in section 974 of the Companies Act) is made by an offeror to acquire all of the shares in the Company not already owned by it and the offeror were to acquire, or unconditionally contract to acquire, not less than 90 per cent in value of the shares to which such offer relates, the offeror could then compulsorily acquire the remaining shares. The offeror would do so by sending a notice to the outstanding members informing them that it will compulsorily acquire their shares and, six weeks later, it would deliver a transfer of the outstanding shares in its favour to the Company which would execute the transfers on behalf of the relevant members, and pay the consideration for the outstanding shares to the Company which would hold the consideration on trust for the relevant members. The consideration offered to the members whose shares are compulsorily acquired under this procedure must, in general, be the same as the consideration that was available under the original offer unless a member can show that the offer value is unfair.

6.3 *Sell-out rules*

The Companies Act also gives minority members a right to be bought out in certain circumstances by an offeror who has made a takeover offer. If a takeover offer related to all the shares in the Company and, at any time before the end of the period within which the offer could be accepted, the offeror held or had agreed to acquire not less than 90 per cent in value of the shares and not less than 90 per cent of the voting rights carried by the shares in the Company, any holder of shares to which the offer related who had not accepted the offer could by a written communication to the offeror require it to acquire those shares. The offeror would be required to give any member notice of his/her right to be bought out within one month of that right arising. The offeror may impose a time limit on the rights of minority members to be bought out, but that period cannot end less than three months after the end of the acceptance period or, if later, three months from the date on which notice is served on members notifying them of their sell-out rights. If a member exercises his/her rights, the offeror is entitled and bound to acquire those shares on the terms of the offer or on such other terms as may be agreed.

7. **Subsidiary undertakings**

With effect from completion of the Share for Share Exchange, the Company has been the holding company of the Group, and the Company has the following significant subsidiary undertakings:

Name	Jurisdiction of incorporation	Proportion of ownership interest (%)	Principal activity
Acacia Pharma Limited.....	UK	100	Research, Development and Commercialisation of Pharmaceuticals
Acacia Pharma Inc.	Delaware, US	100	Sales and Marketing of Pharmaceuticals

8. **Interests of Major Shareholders**

8.1 *Major Shareholders*

In so far as was known to the Company as at the Latest Practicable Date, the following persons were directly or indirectly interested in three per cent or more of the issued share capital of the Company.

Shareholder	Number of Ordinary Shares	Percentage of voting rights (%)
Cosmo	17,500,140	24.05
Gilde.....	16,943,822	23.28
Lundbeckfond.....	12,468,955	17.13
F-Prime.....	3,692,446	5.07
Axa Investment Managers	2,650,846	3.64

None of the Shareholders referred to in this paragraph intends to subscribe for any New Ordinary Shares pursuant to the Fundraising.

None of the Shareholders referred to in this Section has different voting rights from any other holders of Ordinary Shares.

8.2 *Other disclosures relating to Shareholders*

(a) The Company is not aware of any persons who, as at the Latest Practicable Date and immediately after Admission, directly or indirectly, jointly or severally, will exercise or could exercise control over the Company.

(b) The Ordinary Shares are the only class of share capital of the Company. All Shareholders will have equal voting rights and none of the Existing Shareholders will have different voting rights to the holders of New Ordinary Shares.

(c) The Company and the Directors are not aware of any arrangements, the operation of which may, at a subsequent date result in a change in control of the Company.

9. Directors and Senior Managers

9.1 *Directorships and partnerships of the Directors and the Senior Managers outside the Group*

Details of those companies and partnerships outside the Group of which the Directors and the Senior Managers are currently directors or partners, or have been directors or partners at any time during the five years prior to the date of this Prospectus, are as follows:

Director/Senior Manager	Position	Company/Partnership	Position Currently Held
Mike Bolinder	—	—	—
Scott Byrd	President, Chief Executive Officer	Outpost Medicine LLC	Yes
	President, Chief Executive Officer	Pioneer Therapeutics Inc.	Yes
	Entrepeneur-In-Resident	Frazier Healthcare Partners	Yes
	Senior Vice President and Chief Commercial Officer	Cadence Pharmaceuticals, Inc	No
Dr John Brown	Chairman	Cell Therapy Catapult Ltd	Yes
	Chairman	BioCity Nottingham Ltd	Yes
	Chairman	Sympromics Ltd	No
	Non-Executive Director	YourGene Health plc	Yes
	Non-Executive Director	Quantum Pharma plc	No
	Senior independent director	Electrical Geodesics Inc	No
	Chairman	Kyowa Kirin International plc	No
	Chairman	Touch Bionics Ltd	No
	Chairman	Mode Diagnostics Ltd	No
	Senior independent director	Vectura Group plc	No
	Chairman	Scottish LifeSciences Association	No
	Chairman	CXR Ltd	No
	Chairman	BioIndustry Association	No
Edward J. Borkowski	Executive Vice President	Therapeutics HD	Yes
	Director	Co-Diagnostics, Inc	No
	Non-Executive Director and Chairman	AzurRx BioPharma Inc	No
	Non-Executive Director	WhereverTV Broadcasting Corp	No
	Executive Vice President	Concordia International Corp	No
	Chief Financial Officer	Amerigen Pharmaceuticals Limited	No
	Executive Vice President and Interim Chief Financial Officer	MiMedx Group Inc	No
	Chief Financial Officer	ACETO Corporation	No
Alessandro Della Chà	Chief Executive Officer	Cosmo Pharmaceuticals NV	Yes
Dr Gabriel Fox	Director	Comedica Consulting Ltd	Yes
Gary Gemignani	—	—	—

9.2 *Conflicts of interest*

Alessandro Della Chà is also a director of Cosmo Pharmaceuticals N.V., the parent company of Cosmo, a significant Shareholder. The Board has approved those conflicts of interest which have arisen, or which may arise in the future, as a result of Alessandro's and current relationships with Cosmo.

Save as set out above, no Director or Senior Manager has any potential conflict of interest between their duties to the Company and their private interests and/or their duties to third parties.

9.3 *Confirmations by the Directors and the Senior Managers*

As at the date of this Prospectus, save as set out below, no Director or Senior Manager has during the last five years:

(a) been convicted in relation to fraudulent offences;

(b) been associated with any bankruptcy, receivership or liquidation while acting in the capacity of a member of the administrative, management or supervisory body of or senior manager of any company;

(c) been subject to any official public incrimination and/or sanctions by any statutory or regulatory authorities including, where relevant, designated professional bodies; or

(d) been disqualified by a court from acting as a member of the administrative, management or supervisory body of an issuer or from acting in the management or conduct of the affairs of any issuer.

The Group's CFO, Gary Gemignani, previously held the position of CFO of Synergy Pharmaceuticals Inc. ("**Synergy**") from April 2017 to May 2019. In December 2018, Synergy initiated voluntary proceedings under Chapter 11 of the US Bankruptcy Code in the US Bankruptcy Court for the Southern District of New York (the "**Bankruptcy Court**") to facilitate a sale and address its debt obligations. In 2019, Synergy's assets were sold to Bausch Health Companies and the Bankruptcy Court approved its Chapter 11 plan and established a litigation trust. Synergy and/or a number of its former officers and directors (including Mr. Gemignani) are also named in three putative class action lawsuits, brought under the federal securities laws by former Synergy stockholders; those actions are pending in the US District Court for the Eastern District of New York. The court is considering a motion to consolidate the three cases, and Mr. Gemignani and the other former Synergy officers and directors have informed the Court that they intend to move to dismiss the remaining case or cases after that motion is decided.

9.4 *Interests in the share capital of the Company of the Directors and the Senior Managers*

The direct and indirect interests of the Directors and the Senior Managers in the Ordinary Shares at the Latest Practicable Date are set out in the table below.

Name	**No. of Ordinary Shares**	**Percentage of total issued share capital of the Company (%)**
Directors		
Alessandro Della Chà	35,000	0.05
Senior Managers		
Dr Gabriel Fox	497,227	0.68
Total	532,227	0.73

In addition to the interests in Ordinary Shares described above, the Directors and Senior Managers will be interested in options to acquire and awards of Ordinary Shares under the Acacia Pharma Group plc 2015 Enterprise Management Incentive Plan (the "**EMI Plan**"), the Acacia Pharma Group plc 2015 Discretionary Share Option Plan (the "**2015 Plan**") and the Acacia Pharma Group Performance Share plan (the "**PSP**"), as set out below:

	Plan	Granted	Number Held	Exercise Price	Exercisable
Executive Directors & Senior Managers					
Michael Bolinder	2015	28-Aug-15	50,000	200p	Now
Michael Bolinder	2015	30-Dec-16	1,500	2p	Now
Michael Bolinder	2015	31-Oct-17	100,000	200p	30-Oct-20
Michael Bolinder	PSP	18-Dec-18	90,000	0	Note 1
Michael Bolinder	PSP	19-Mar-18	60,000	2p	Note 1
Michael Bolinder	PSP	18-Jul-19*	75,000	2p	Note 2
Michael Bolinder	PSP	18-Jul-19*	175,000	2p	Note 3
Michael Bolinder	PSP	18-Jul-19*	100,000	2p	Note 4
Gabriel Fox	EMI	04-Jul-11	235,829	10p	Now
Gabriel Fox	EMI	07-Mar-12	62,000	10p	Now
Gabriel Fox	EMI	22-Oct-13	76,515	10p	Now
Gabriel Fox	EMI	22-Oct-13	311,114	10p	Now
Gabriel Fox	EMI	04-Apr-14	213,580	2p	Now
Gabriel Fox	EMI	30-Dec-16	3,750	2p	Now
Gabriel Fox	PSP	19-Mar-18	71,875	2p	Note 1
Gabriel Fox	PSP	18-Jul-19	50,000	2p	Note 2
Gabriel Fox	PSP	18-Jul-19	45,000	2p	Note 3
Gabriel Fox	PSP	18-Jul-19	70,000	2p	Note 4
Gary Gemignani	PSP	01-Jan-20	400,000	0	Note 6
Non-Executive Directors					
Scott Byrd	PSP	18-Jul-19*	6,125	2p	Note 2
Scott Byrd	2015	28-Aug-15	111,000	2p	Now
Scott Byrd	2015	28-Aug-15	139,000	200p	Now
John Brown	PSP	18-Jul-19*	7,290	2p	Note 2
Edward Borkowski	PSP	18-Jul-19*	6,855	2p	Note 2

* Awards granted on 18 July 2019, effective as of 5 September 2019.

The Non-Executive Directors are also interested in share options which were granted to them in return for foregoing 50 per cent of their cash Directors' fees until approval of BARHEMSYS®.

Non-Executive Directors	Granted	Number Held	Exercise Price	Exercisable
Scott Byrd	18-Jul-19	6,125	2p	Note 5
John Brown	18-Jul-19	7,290	2p	Note 5
Edward Borkowski	18-Jul-19	6,855	2p	Note 5

Note 1

Awards as set out below were made under the PSP on 19 March 2018 in the form of options, exercisable at 2p per Share, vesting in March 2021 and subject to performance conditions. The performance conditions for the 2018 PSP awards provide that 25 per cent of each award will be measured against an absolute target for Total Shareholder Return ("**TSR**") to the end of 2020, 37.5 per cent against progress in securing acceptance for BARHEMSYS® on hospital formularies by the end of 2020 and 37.5 per cent against 2020 revenues. Michael Bolinder received options over 60,000 Shares, Christine Soden received options over 75,000 Shares and Gabriel Fox received options over 71,875 Shares. In December 2018, an award was made over 90,000 Shares to Michael Bolinder in the form of a conditional award of Shares, conditional upon him remaining in his position at 31 December 2021.

Note 2

Following receipt of the CRL for BARHEMSYS® in May 2019, the Remuneration Committee (in consultation with the Company's two largest Shareholders), agreed to grant a number of PSP awards in lieu of certain employees and Directors foregoing up to 50 per cent of their salary and foregoing any rights to cash bonus payments for 2019 in order to preserve cash resources, minimise the need to reduce headcount and secure retention. The grant of these awards is subject to approval by Shareholders at the Company's annual general meeting in 2020. The vesting of these awards was conditional upon receiving the BARHEMSYS® NDA on or before 30 June 2020. They can be exercised on publication of the next interim or annual financial results of the Group following the earlier of the Company obtaining sufficient finance to recruit a salesforce of at least 30 representatives or 1 year after BARHEMSYS® NDA approval.

Note 3

In line with competitive practice in the US, where most of the Group's employees are based, awards were granted that vest as to one third after one year with the remainder as to 1/24th per month over the following two years from grant provided the recipient remains employed by the Group but cannot ordinarily be exercised until the third anniversary of grant. The grant of these awards is subject to approval by Shareholders at the Company's annual general meeting in 2020.

Note 4

The vesting of these awards is conditional upon meeting certain performance criteria over the 3 years ending 31 December 2021: (i) one third vest subject to TSR performance from 1 January 2019 to 31 December 2021 (the threshold TSR is 7.5 per cent per annum with a maximum award if 25 per cent TSR per annum is achieved); (ii) one third vest depending on achieving certain cumulative revenues to 31 December 2021 (there is no award if cumulative revenues are less than $50 million and the maximum award will be granted if cumulative revenues are $80 million or greater); and (iii) one third vest based upon achieving certain cumulative funding by 31 December 2021 (there is no award if cumulative funding is less than $80 million and the maximum award will be granted if cumulative fundraising is $120 million or greater).

Note 5

These awards vested upon the NDA for BARHEMSYS® receiving approval and become exercisable after the Company obtains sufficient finance to recruit a sales force of at least 30 representatives.

Note 6

In line with competitive practice in the US, 340,000 awards were granted that vest as to one third after one year, one third after two years, and the remaining third after three years. The remaining 60,000 awards vest upon receiving the BARHEMSYS® NDA on or before 30 June 2020. They can be exercised on publication of the next interim or annual financial results of the Group following the earlier of the Company obtaining sufficient finance to recruit a salesforce of at least 30 representatives or 1 year after BARHEMSYS® NDA approval.

Save as set out above, no Director or Senior Manager has any interests (beneficial or non-beneficial) in the share capital of the Company or any other securities of the Company.

9.5 *Transactions with Directors and Senior Managers*

None of the Directors or Senior Managers has or has had any interest in any transaction which is or was unusual in its nature or conditions or significant to the business which was effected by any member of the Group during the current or immediately preceding financial year, or which was effected during an earlier financial year, and remains in any respect outstanding or unperformed.

None of the Directors or Senior Managers has or had a beneficial interest in any contract to which any member of the Group was a party during the current or immediately preceding financial year.

9.6 *Executive Director's service contract, remuneration and emoluments*

The Company has entered into a service agreement with Mike Bolinder as Chief Executive Officer. The principal terms of the agreement is set out below. The Company currently has no other Executive Directors.

(a) General terms

The annual salary of the Chief Executive Officer is $594,000 per annum. This salary will be reviewed, but not necessarily increased, in or about the month of January each year.

The Executive Director is expected to devote the whole of his working time, attention and abilities to the duties assigned to him (save for fulfilling any external non-executive directorships or advisory roles that the Board may from time to time allow) and in return the Executive Director will receive the following benefits under the terms of his service agreement:

(i) entitlement to a discretionary performance-related annual bonus, any deferred element of which will be granted under the terms of the DABP as described in Section 10.2 of this Part XIV (*Additional Information*);

(ii) eligibility to participate in the same benefits package as the other US employees of the Group, including its private health insurance scheme;

(iii) eligibility to participate in the PSP described in Section 10.2 of this Part XIV (*Additional Information*);

(iv) in the event of sickness absence, entitlement to receive payment of full salary and contractual benefits for up to 90 days in any 12 month period; and

(v) a minimum of 20 days' paid time off, in line with the policy applying to all US employees.

In addition, the Executive Director will be entitled to reimbursement of reasonable expenses incurred in the course of his duties and to the benefit of directors' and officers' liability insurance with an indemnity limit of £2 million, maintained by the Company on his behalf.

(b) Termination provisions

The service agreement of the Executive Director is an at-will employment agreement and can be terminated by either party at any time for any reason with or without notice. If the Executive Director's employment is terminated by the Company without cause or by the Executive for good reason, the Executive shall be entitled to receive his fully earned unpaid salary through the date of termination, a lump-sum cash payment

equal to 100% of his annual base salary, payment by the Company of the employer portion of his health insurance premiums for 12 months, and a pro rated payment of his target annual bonus for the year in which his employment terminated.

The employment of the Executive Director will be terminable with immediate effect and without notice or payment in lieu of notice in certain circumstances. Such circumstances include where he is guilty of gross misconduct or a material breach of his obligations, commits and fails to remedy a breach of his service agreement, becomes bankrupt, is convicted of a criminal offence (excluding certain road traffic offences for which a fine or non-custodial penalty is imposed), is disqualified from holding office, is guilty of financial dishonesty, becomes of unsound mind, fails after investigation to perform his duties to a satisfactory standard, brings the name of himself, the Company or any member of the Group into disrepute, is prevented by illness or injury from performing his obligations for an aggregate of 90 working days in any twelve month period, is guilty of a breach of the Bribery Act 2010, is guilty of a serious breach of any rules issued by the Company or any member of the Group, or abuses alcohol or drugs in such a manner as to affect the Executive Director's ability to perform his duties under the service agreement.

The Executive Director's service agreement also contain post-termination restrictions. These restrictions include: (i) a six month restriction on soliciting clients; (ii) a six month restriction on offering to employ or engage key employees of the Group; (iii) a three month restriction on competing with the Group; and (iv) a prohibition on holding himself out as connected with the Group at any time following termination.

9.7 *Non-Executive Directors' letters of appointment and fees*

The Company has four Non-Executive Directors. Scott Byrd, Dr John Brown and Edward J. Borkowski are all independent Non-Executive Directors.

The Non-Executive Directors are appointed by letters of appointment and do not have service agreements. The principal terms of these letters of appointment are set out below.

(a) General terms

Each Non-Executive Director is entitled to an annual fee. The level of these fees will be reviewed periodically by the Board. The fee levels that currently apply are set out in the table below.

Name	Annual Fee	Committee Chairmanship	Committee Chair Fee
Scott Byrd	£115,000	Nomination Committee	None
Dr John Brown	£45,000*	Remuneration Committee	£5,000
Edward J. Borkowski	£42,000	Audit Committee	£5,000
Alessandro Della Chà	£42,000	None	None

* Includes fee of £3,000 as Senior Independent Director.

In addition, the Non-Executive Directors are entitled to be reimbursed for all reasonable expenses incurred by them in the course of their duties to the Company and have the benefit of indemnity insurance maintained by the Company on their behalf.

Each letter of appointment contains obligations of confidentiality which have effect during the appointment and after termination.

(b) Term

The Company has appointed each Non-Executive Director for an initial period of three years and in each case the appointment is terminable by either the Non-Executive Director or the Company on three months' notice, and the Company is entitled to make a payment in lieu of their notice period on termination.

9.8 *Directors' and Senior Managers' remuneration in 2019*

In 2019, the aggregate amount of remuneration paid (including salary and other emoluments but excluding share-based payments) and benefits in kind granted to the Directors and the Senior Managers for services in all capacities to the Group was $1,135,000.

In 2019, the Directors were remunerated as set out below:

	Salary/ fees $'000	Benefits[2] $'000	Total annual bonus[3] $'000	Share options $'000	Long-term incentives[4] $'000	Pension[5] $'000	Total[6] $'000
Executive Directors							
Mike Bolinder[1]	67	11	—	—	—	—	78
Julian Gilbert[1]	239	4	—	—	—	24	267
Christine Soden[1]	209	—	—	—	—	21	230
Non-Executive Directors							
Patrick Vink	117	—	—	—	—	—	117
Ed Borkowski[8]	48	—	—	—	—	—	48
John Brown[8]	51	—	—	—	—	—	51
Pieter van der Meer	—	—	—	—	—	—	—
Johan Kördel	—	—	—	—	—	—	—
Scott Byrd	43	—	—	—	—	—	43

1. Remuneration shown for Mike Bolinder is from 1 August 2019, the date of his appointment as Chief Executive Officer. Remuneration for Julian Gilbert is shown to 31 July 2019, the date he stepped down as Chief Executive Officer. To improve cash flow management while waiting for BARHEMSYS® approval, Christine Soden and Mike Bolinder reduced their salary to 40 per cent from 1 June 2019 and 1 August 2019 respectively. Christine Soden resigned with effect from 29 February 2020.
2. Benefits shown above relate primarily to the provision of private medical benefits, travel and life insurance.
3. No cash bonuses were awarded in 2019, instead, share awards were granted in lieu of bonus opportunity foregone under the 2018 PSP.
4. The first vesting date of long-term incentive plan awards made under the 2018 PSP is 18 March 2021.
5. Pension consists of cash supplement in lieu of employer pension contributions in accordance with the relevant service contracts.
6. Not included in the single figure table are share awards made to Directors following the decision to reduce cash expenditure. These are summarised below and included in the disclosures in Section 9.4 of this Part XIV (*Additional Information*).
   (i) Mike Bolinder. Share awards were granted upon on his promotion to CEO and in lieu of salary and bonus opportunity foregone.
   (ii) Christine Soden. Share awards were granted in lieu of salary and bonus opportunity foregone.
   (iii) Julian Gilbert. Share awards were granted in respect of his continued post-employment advisory services to the Group.
   (iv) Non-Executive Directors. As part of cash flow management, the Non-Executive Directors agreed to reduce their Directors' fees by 50 per cent from 1 August 2019, and to receive share awards in lieu of a cash fee.

9.9 *Remuneration Policy*

(a) Remuneration of the Directors and Senior Managers

The Company's remuneration strategy is to provide a remuneration framework that is appropriate to the markets in which the Company operates that will:

- promote the long-term success of the business;
- attract, retain and motivate executives and senior management in order to deliver the Company's strategic goals and business outputs;
- provide an appropriate balance between fixed and performance related pay supporting a high performance culture;
- provide a simple remuneration structure which is easily understood by all stakeholders;
- adhere to the principles of good corporate governance and appropriate risk management;
- align employees with the interests of Shareholders and other external stakeholders;
- consider the wider pay environment both internally and externally; and
- encourage widespread equity ownership across the Group.

Consistent with this remuneration strategy, the Remuneration Committee has agreed a remuneration policy for the Senior Managers and the Executive Directors.

10. **Share plans and employee incentive schemes**

10.1 *The EMI and 2015 Plan*

Prior to the IPO, the Group operated the EMI and 2015 Plan. No further awards have been (nor will they be) made under the EMI or the 2015 Plan since the IPO.

Participants whose options are or become exercisable in accordance with the rules of the EMI and 2015 Plan may continue to exercise their options over Ordinary Shares. Options which are subject to time vesting will continue to vest according to their current vesting schedules save that the Board deemed that a number

of options would vest at completion of the IPO. Unless exercised, options under the EMI and 2015 Plan will lapse on the tenth anniversary of their date of grant (or their original date of grant under a predecessor plan operated by the Operating Company), to the extent they have not otherwise lapsed in accordance with the rules.

10.2 *The Executive Share Plans*

The Acacia Pharma Group Performance Share Plan (the "**PSP**"), the Acacia Pharma Group Deferred Annual Bonus Plan (the "**DABP**") and the Acacia Pharma Group Company Share Option Plan (the "**CSOP**", and together with the PSP and the DABP known as the "**Executive Share Plans**") cater for discretionary share based incentive awards to selected employees within the Group. The CSOP may be used to grant UK and US tax-advantaged options (known as 'incentive stock options') in accordance with Schedule 4 of the Income Tax (Earnings and Pensions) Act 2003 and section 422 of the Revenue Code respectively.

To the extent that awards are delivered to employees under the PSP and the DABP for nil payment and/or are satisfied using existing shares, the shares used to satisfy such awards may first be sourced via an employees' benefit trust established by the Company or another group company (the "**EBT**").

11. Corporate governance

11.1 *Compliance with the UK Corporate Governance Code 2018*

The Board is committed to the highest standards of corporate governance. As at the date of this Prospectus, the Board considers that it complies with the Code. Until 7 April 2020 however, the Company was not compliant with the Code because (i) at least half of the Directors were not considered independent, (ii) the Chairman sits on the Audit Committee and (iii) a non-independent Director sits on the Remuneration Committee. Given the size of the Group and the experience of the Non-Executive Directors and the uncertainty arising after receipt of the CRL for BARHEMSYS®, the Nomination Committee determined it would be appropriate to wait until 2020 before seeking to address these areas of non-compliance. Following the AGM on 7 April 2020, the Company is compliant with the Code.

11.2 *The Board*

The Company is led and controlled by the Board. The names, responsibilities and details of the current Directors appointed to the Board are set out above in Part VII (*Directors, Senior Managers and Corporate Governance*).

11.3 *Securities dealing code*

The Company has a code on dealings in relation to the securities of the Group. The Company requires the Directors and other persons discharging managerial responsibilities within the Group to comply with the Company's securities dealing code, and takes all proper and reasonable steps to secure their compliance.

12. Pensions

The Company contributes to a money purchase pension scheme for its employees. No amounts have been set aside or accrued by the Group to provide pension, retirement or similar benefits, with all contributions paid to the pension scheme providers by each period end.

13. Employees

The Group has 37 full-time-equivalent employees as at the date of this Prospectus, with up to 80 full-time employees targeted for its US operations by the time of the full launch of BARHEMSYS® and BYFAVO™. If the launches of BARHEMSYS® and BYFAVO™ are successful, the Group expects to expand its sales and marketing infrastructure following launch and further to support the launch of APD403 (assuming it proceeds to commercialisation).

14. Related party transactions

Save as set out in Note 16 to the 2020 Interim Financial Statements which are incorporated by reference as set out in Part XI (*Historical Financial Information*) of this Prospectus, between 30 June 2020 and the date of this Prospectus, no member of the Group entered into any related party transactions (within the meaning ascribed to that term in paragraph 9 of International Accounting Standard 24, being the Standard adopted according to Regulation (EC) No. 1606/2002).

15. **Significant change**

Save as set out below, there has been no significant change in the financial performance or financial position of the Group since 30 June 2020, being the end of the last financial period for which financial information has been published:

- On 2 July 2020, the FDA approved BYFAVO™ for injection for the induction and maintenance of procedural sedation in adults undergoing procedures lasting 30 minutes or less. As a result, the Company was obliged, pursuant to the BYFAVO™ Sub-Licence Agreement, to make a milestone payment to Cosmo of €30 million, which was settled in full in accordance with the terms of the BYFAVO™ Sub-Licence Agreement and the First Cosmo Investment Agreement as follows: (i) by the issue of 4,923,811 Ordinary Shares to Cosmo, which were issued on 16 July 2020; and (ii) by a payment of €15 million in cash, which was paid on 27 July 2020, financed through a drawdown of €15 million on the €25 million Loan Agreement with Cosmo, which had become available to the Group on the approval of BYFAVO™.
- On 13 July 2020, the BYFAVO™ Sub-Licence Agreement was terminated and replaced with (a) the BYFAVO™ Assignment Agreement, and (b) the BYFAVO™ Wind-Up Agreement. The BYFAVO™ Assignment Agreement became effective on 7 August 2020.
- On 27 July 2020, the FDA approved a second supplier for the API for BARHEMSYS® (amisulpride injection).

Further details of the BYFAVO™ Sub-Licence Agreement, the BYFAVO™ Assignment Agreement, the BYFAVO™ Wind-up Agreement, the First Cosmo Investment Agreement and the €25 million Loan Agreement are set out in Section 18 of this Part XIV (*Additional Information*) of this Prospectus.

16. **Working capital statement**

The Company is of the opinion that the Group has sufficient working capital for its present requirements, that is for at least the 12 months from the date of publication of this Prospectus, taking into account the net proceeds of the Fundraising.

17. **Litigation and disputes**

There are no governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which the Company is aware) during the 12 months preceding the date of this document which may have or have had in the recent past significant effects on the Company and/or Group's financial position or profitability.

18. **Material contracts**

Set out below is a summary of (i) each material contract (other than a contract entered into in the ordinary course of business) to which the Company or any member of the Group is a party which has been entered into within the two years immediately preceding the date of this Prospectus; and (ii) any other contract (other than a contract entered into in the ordinary course of business) entered into by any member of the Group which contains obligations or entitlements which are or may be material to the Group as at the date of this Prospectus.

18.1 *Placing Agreement*

The Company, the Directors and the Banks have entered into the Placing Agreement pursuant to which, on the terms and subject to certain conditions contained therein (which are customary in agreements of this nature), Jefferies and Guggenheim Securities have agreed, as agents for the Company, severally to use reasonable endeavours to procure placees for the New Ordinary Shares within the United States, the United Kingdom and elsewhere outside the European Union and Jefferies and Degroof Petercam have agreed, as agents for the Company, severally to use reasonable endeavours to procure placees for the New Ordinary Shares in the United States, the European Union and the United Kingdom. Bank Degroof Petercam SA/NV is not a US-registered broker-dealer; therefore, to the extent that it intends to effect any sales of the shares in the United States, it will do so through Global Alliance Securities, LLC, its affiliated US-registered broker-dealer, in accordance with the SEC Rule 15a-6, and as permitted by FINRA regulations. The Fundraising is being underwritten by the Banks, subject to the terms and conditions set out in the Placing Agreement. To the extent that any placee procured by the Banks fails to subscribe for any or all of the New Ordinary Shares allotted to it, the Banks shall themselves subscribe for such New Ordinary Shares at

the Placing Price. In such circumstances, each Bank shall be required to subscribe for such New Ordinary Shares at the Placing Price only in respect of the placees it has procured.

The Fundraising is conditional upon, *inter alia*, Admission of the New Ordinary Shares occurring not later than 8:00 a.m. CET on 18 August 2020 (or such later date or time as the Banks and the Company may agree) and the Placing Agreement becoming unconditional in all respects and not having been terminated in accordance with its terms.

The Placing Agreement can be terminated at any time prior to Admission of the New Ordinary Shares in certain customary circumstances set out therein. If these termination rights are exercised, the Fundraising will lapse and any monies received in respect of the Fundraising will be returned to applicants without interest. The Company has given customary warranties and indemnities to the Banks which are customary for an agreement of this nature.

The Placing Agreement provides for the Banks to be paid a commission in respect of the New Ordinary Shares for which placees are procured. Any commissions received by the Banks may be retained. The Company has agreed to pay or cause to be paid (together with any applicable VAT) certain costs, charges, fees and expenses of or arising in connection with or incidental to, the Fundraising.

Allocations of the New Ordinary Shares among prospective investors will be determined by the Company in consultation and jointly agreed with the Banks.

Pursuant to the Placing Agreement, the Company has agreed that during the period of 90 days from the date of Admission, it will not without the prior written consent of Jefferies and Guggenheim Securities, (a) directly or indirectly, issue, offer, allot, lend, sell, contract to sell or issue, grant any option, right or warrant to subscribe or purchase or allow any Encumbrance to be created over or otherwise dispose of, directly or indirectly, any Shares (or any securities convertible into or exchangeable for Shares or which carry rights to subscribe or purchase Shares) or any interest (within the meaning of section 820 of CA 2006) in any Shares or enter into any transaction with the same economic effect as, or agree to do, any of such things; or (b) publicly announce any intention to do any of such things.

The Placing Agreement is governed by the laws of England and Wales.

18.2 *Lock-up Agreements*

On 11 August 2020, each of the Directors, Senior Managers and Cosmo entered into a Lock-Up Agreement. Under the terms of the Lock-Up Agreements each of the Directors, Senior Managers and Cosmo has agreed that, subject to certain exceptions, during the period commencing on the date of Admission and ending on the date 90 days from the date of Admission, he or it will not, without the prior written consent of Jefferies and Guggenheim Securities, (a) offer, sell, assign, transfer, contract to offer, sell, assign, transfer, pledge (unless such pledged shares cannot be sold within the 90 day period referred to above) or otherwise transfer or dispose of, directly or indirectly, any Ordinary Shares or securities convertible or exchangeable into or exercisable for Ordinary Shares or warrants or other rights to subscribe for Ordinary Shares, or enter into any derivative or other transaction having substantially similar economic effect with respect to the Ordinary Shares or any such securities or (b) announce publicly its intention to do any of the foregoing. The Lock-up Agreements are governed by English law.

18.3 *BYFAVO™ Acquisition*

On 10 January 2020, the Company and the Operating Company entered into a sub-licence agreement with Cosmo (the "**BYFAVO™ Sub-Licence Agreement**") pursuant to which the Operating Company was granted an exclusive sub-licence by Cosmo, who in turn held a licence granted by Paion (a wholly-owned subsidiary of Paion AG) dated 24 June 2016 (the "**BYFAVO™ Head Licence Agreement**"). Under and from the date of this agreement, Cosmo granted all its material rights and imposed all its material obligations under the BYFAVO™ Head Licence Agreement to the Operating Company. This included (i) the grant of the rights to further develop, commercialise and manufacture BYFAVO™ in the US including its non-state territories; (ii) the right (but not the obligation) to manage the prosecution of patents for the US including its non-state territories; (iii) the obligation to obtain and maintain regulatory approvals, and (iv) the obligation to use commercially reasonable effects in the commercialisation of BYFAVO™ in the US and its non-state territories.

The consideration for the sub-licence included: (i) payment of €10 million, which was satisfied by the issue of new Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the execution of the agreement, being €2.152 per share (the "**Initial Consideration**"); (ii) payment of €30 million upon approval of BYFAVO™ by the FDA, which was settled

in full as follows: (a) by the issue of 4,923,811 Ordinary Shares issued at €3.046 per Ordinary Share, which were issued on 16 July 2020, plus (b) €15 million in cash paid on 27 July 2020; (iii) payment of €5 million upon the first commercial sale of BYFAVO™ by the Operating Company, which is expected to be satisfied by the issue of New Ordinary Shares issued at the average of the volume weighted middle market price of the Ordinary Shares for the 15 trading days prior to the date of the first commercial sale of BYFAVO™ by the Operating Company; (iv) US$5 million in cash upon the Operating Company first achieving US$50 million in annual "net sales" (being gross sales less returns, customary discounts and chargebacks); (v) US$10 million in cash upon the Operating Company first achieving US$100 million in annual net sales; (vi) US$15 million in cash upon the Operating Company first achieving US$150 million in annual net sales; (vii) US$20 million in cash upon the Operating Company first achieving US$200 million in annual net sales; (viii) US$25 million in cash upon the Operating Company first achieving US$250 million in annual net sales; (ix) US$30 million in cash upon the Operating Company first achieving US$300 million in annual net sales; (x) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a second indication; and (xi) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a third indication.

18.4 *Amendments to the BYFAVO Licensing Arrangements*

On 13 July 2020, the Company and the Operating Company entered into an assignment agreement between Paion, Cosmo and the Operating Company (the "**BYFAVO™ Assignment Agreement**"). On 15 July 2020, the Company, the Operating Company and Cosmo entered into a wind-up agreement in order to terminate the BYFAVO™ Sub-Licence Agreement (the "**BYFAVO™ Wind-Up Agreement**"). The BYFAVO™ Assignment Agreement and the BYFAVO™ Wind-Up Agreement became effective on 7 August 2020.

The BYFAVO™ Assignment Agreement assigned to Acacia the entirety of Cosmo's rights and obligations under the BYFAVO™ Head-Licence Agreement. The BYFAVO™ Wind-Up Agreement terminated the BYFAVO™ Sub-Licence Agreement and specified which rights and obligations that survive as between Cosmo, the Operating Company and the Company. There are no material changes to the Operating Company's rights and obligations as compared to the position during the term of the BYFAVO™ Sub-Licence Agreement, except that many of such rights and obligations will be enforceable against or by Paion instead of Cosmo. The consideration referred to in the paragraph above entitled "*18.3 BYFAVO™ Acquisition*" remains due to Cosmo under the terms of the BYFAVO™ Wind-Up Agreement, except for the following which shall become due directly to Paion: (x) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a second indication; and (xi) €10 million in cash upon the Operating Company obtaining approval of BYFAVO™ by the FDA for a third indication.

A further description of the terms and condition of the BYFAVO™ Assignment Agreement and the BYFAVO™ Wind-Up Agreement are below:

(a) The BYFAVO Assignment Agreement

The BYFAVO™ Assignment Agreement operates to assign the rights and obligations of Cosmo from and to Paion under the BYFAVO™ Head Licence Agreement to the Operating Company (such rights and obligations being those discussed in Section 18.3 above) with effect from 7 August 2020. This replaced the previous arrangements under the BYFAVO™ Sub-Licence Agreement where those rights and obligations were granted to or imposed upon the Operating Company by Cosmo.

In addition, the BYFAVO™ Assignment Agreement includes the assignment by Cosmo to the Operating Company of the US trade mark applications for BYFAVO™ with effect from 7 August 2020.

Under the BYFAVO™ Assignment Agreement, royalties on net sales of BYFAVO™ shall be payable to Paion by the Operating Company of (i) 20 per cent of net sales per calendar year up to a total amount of net sales of US$200 million; (ii) 25 per cent of net sales per calendar year for net sales exceeding US$200 million (on the amount exceeding US$200 million); and (iii) 10 per cent of net sales per calendar year after the expiration of the last-to expire licensed patent and as long as the Operating Company enjoys market exclusivity.

(b) BYFAVO™ Wind-Up Agreement

The BYFAVO™ Wind Up Agreement terminated the BYFAVO™ Sub-Licence Agreement with effect from 7 August 2020, which became necessary because Cosmo would no longer be in a position to grant a sub-licence to BYFAVO™ following the BYFAVO™ Assignment Agreement becoming effective. The BYFAVO™ Wind-Up Agreement specifies which rights and obligations from the BYFAVO™ Sub-Licence Agreement survive as between Cosmo, the Operating Company and the Company. These include obligations of Acacia

to pay Cosmo the milestone payments referred to in Section 18.3 above (except (x) and (xi) which shall be payable directly to Paion under the BYFAVO™ Assignment Agreement), the obligations of Cosmo relating to the assignment to the Operating Company of its existing manufacturing arrangements for BYFAVO™ and the transfer of its existing know-how, as well as mutual obligations in relation to confidential information.

The BYFAVO™ Assignment Agreement and the BYFAVO™ Wind-Up Agreement are each governed by German law.

18.5 *First Cosmo Investment Agreement*

On 10 January 2020, the Company entered into an investment agreement with Cosmo pursuant to which Cosmo subscribed for 4,646,841 Ordinary Shares in satisfaction of the Initial Consideration payable under the BYFAVO™ Sub-Licence Agreement. Cosmo further subscribed for 4,347,826 New Ordinary Shares for cash at a price of €2.300 per Ordinary Share.

As noted in the BYFAVO™ Sub-Licence Agreement, upon approval of BYFAVO™ by the FDA, the Company was required to issue to Cosmo such number of Ordinary Shares issued at a price per share of the volume weighted average price of the 15 trading days prior to such approval as is equal to €15 million (which equated to issue of 4,923,811 Ordinary Shares issued at €3.046 per Ordinary Share and which were issued on 16 July 2020).

As further noted in the BYFAVO™ Wind-Up Agreement, upon the first commercial sale of BYFAVO™ by the Operating Company, the Company shall, within 10 business days, issue to Cosmo such number of Ordinary Shares issued at a price per share of the volume weighted average price of the 15 trading days prior to the date of the first commercial sale of BYFAVO™ by the Operating Company as is equal to €5 million.

Cosmo agreed that, subject to certain exceptions, during the period of six months from the issue of any Ordinary Shares pursuant to the First Cosmo Investment Agreement, it would not, without the prior written consent of the Company, lend, mortgage, assign, offer, sell or contract to sell or otherwise dispose of any such Ordinary Shares (or any interest therein or in respect thereof) or enter into any transaction with the same economic effect as any of the foregoing. This lock-up period has expired in respect of the Ordinary Shares issued as the Initial Consideration, will expire on 16 January 2021 in respect of the Ordinary Shares issued on BYFAVO™ Approval and will expire six months from the issue of any Ordinary Shares issued pursuant to the milestone payment payable on the first commercial sale of BYFAVO™ by the Operating Company.

For so long as Cosmo holds, whether directly or indirectly, at least 10 per cent of the Company's issued share capital, the Company has granted Cosmo the right to appoint an individual to act as a Director of the Company.

The First Cosmo Investment Agreement is governed by English law.

18.6 *Cosmo Loan Agreements*

(a) €10 million Loan Agreement

On 10 January 2020, the Company and the Operating Company entered into a loan agreement with Cosmo pursuant to which, conditional on the approval of BARHEMSYS® by the FDA, Cosmo agreed to advance up to €10 million to the Operating Company by way of an unsecured loan (the "**€10 million Loan Agreement**"). The €10 million Loan Agreement was terminated pursuant to the Deed of Termination and Release described in Section 18.10 below and Cosmo subscribed for €10 million of Ordinary Shares as described in the Second Cosmo Investment Agreement described in Section 18.9 below.

(b) €25 million Loan Agreement

On 10 January 2020 (as amended by an amendment agreement dated 22 June 2020) the Company and the Operating Company entered into a second loan agreement with Cosmo (the "**€25 million Loan Agreement**") pursuant to which, conditional on the approval of BYFAVO™ by the FDA, Cosmo agreed to advance up to €25 million to the Operating Company by way of an unsecured loan. The amendment agreement dated 22 June 2020 amended the original availability period for drawdown of the loan, which spanned the period from the date of FDA approval of BYFAVO™ to 18 May 2020, to a revised arrangement such that monies are available for drawdown in up to two tranches, with the first tranche of €15 million drawn down on 27 July 2020 and the second tranche of €10 million available for drawdown until 30 September 2020. As at the date of the Prospectus, the Operating Company has drawn down €15 million under this loan and the remaining €10 million available is undrawn. Drawdowns under the

agreement are subject to the customary conditions precedent, unless waived by Cosmo, such as certain warranties being correct and delivery of certain certifications and corporate documentation. These remaining funds available for drawdown are expected to be drawn by 30 September 2020 and used for the purposes of launching BARHEMSYS® and BYFAVO™ in the United States.

The €25 million Loan Agreement is unsecured and subordinated to the Hercules Facility (as defined below) and interest will accrue, daily on the amount drawn and payable monthly, at the rate of 11 per cent per annum until the Company has discharged the Hercules Facility. Once security is released under the Hercules Facility, certain security, including fixed and floating charges over all or substantially all of the assets of each member of the Group, will be pledged under the €25 million Loan Agreement and interest will be reduced to 9 per cent per annum. The loan will be repayable in 24 equal monthly instalments commencing in July 2023. The Group has agreed to pay all costs, fees and expenses relating to amendments or extensions of the €25 million Loan Agreement and is required to pay certain taxes in connection with the €25 million Loan Agreement.

In connection with the €25 million Loan Agreement, the Company and the Operating Company make customary representations and warranties to Cosmo. The €25 million Loan Agreement also imposes certain customary restrictive covenants, including those requiring that the Group:

- report to Cosmo of annual audited financial information;
- inform Cosmo of any litigation or any claims that arise;
- obtain and maintain all consents or authorizations necessary to perform the €25 million Loan Agreement;
- notify Cosmo of any potential event of default or event of default under the €25 million Loan Agreement;
- conduct its business in a proper and efficient manner;
- not incur indebtedness with more advantageous terms than those of the €25 million Loan Agreement without prior consent of Cosmo, subject to certain limited exceptions, such as those relating to the Group's ordinary course of business and the Hercules Facility;
- not provide security, subject to similar customary exceptions; and
- not dispose of any assets, or parts thereof, without Cosmo's prior consent.

The Cosmo Loan Agreements are governed by English law.

18.7 *Cosmo Guarantees*

On 10 January 2020, the Company and the US Subsidiary entered into two guarantees with Cosmo in respect of each of the Cosmo Loan Agreements. Under each guarantee, the Company and the US Subsidiary irrevocably and unconditionally, joint and severally, guarantee to Cosmo punctual performance of all the obligations under the Cosmo Loan Agreements and undertake that where payment is not made by the Operating Company under the Cosmo Loan Agreements, they shall immediately on demand pay such amount. The Cosmo Guarantee in respect of the €10 million Loan Agreement was terminated pursuant to the Deed of Termination and Release described in Section 18.10 below.

The Cosmo Guarantees are governed by English law.

18.8 *Subordination Agreement*

On 10 January 2020, the US Subsidiary, the Company, the Operating Company (together, the "**Loan Parties**"), Hercules Capital and Cosmo entered into a subordination agreement in which Cosmo agreed to subordinate: (i) all of each Loan Parties' indebtedness and obligations to it to all of the Loan Parties' indebtedness and obligations to Hercules; and (ii) all of its security interests, if any, in the Loan Parties' property to all of Hercules' security interests in the Loan Parties' property, for so long as any amounts under the Hercules Facility (described below) remain outstanding. Please see Section 18.11 for a description of the Hercules Facility.

The Subordination Agreement is governed by the laws of the State of California.

18.9 *Second Cosmo Investment Agreement*

On 30 May 2020, the Company entered into an investment agreement with Cosmo pursuant to which, in consideration for and conditional upon Cosmo agreeing to enter into the Deed of Termination and Release,

the Company agreed to pay Cosmo a sum of €1,100,000 which was satisfied by the issue to Cosmo of 367,893 Ordinary Shares. In addition, Cosmo further agreed to subscribe for 3,213,769 Ordinary Shares for cash at a price of €3.112 per Ordinary Share.

Cosmo agreed that, subject to certain exceptions, during the period of six months from their issue, it will not, without the prior written consent of the Company, lend, mortgage, assign, offer, sell or contract to sell or otherwise dispose of any Ordinary Shares (or any interest therein or in respect thereof) or enter into any transaction with the same economic effect as any of the foregoing.

The Second Cosmo Investment Agreement is governed by English law.

18.10 *Deed of Termination and Release*

On 30 May 2020, the Company, the Operating Company and the US Subsidiary entered into a deed of termination and release with Cosmo pursuant to which, conditional on the Second Cosmo Investment Agreement becoming effective, each party released and discharged each other party from all claims and demands under the €10 million Loan Agreement and the associated Cosmo Guarantee.

The Deed of Termination and Release is governed by English law.

18.11 *Hercules Facility*

On 29 June 2018, the US Subsidiary, as borrower, and the Company and the Operating Company, as guarantors, entered into a loan and security agreement with Hercules Capital as agent and as lender, for a term loan facility in principal amount of up to $30 million (the "**Hercules Facility**"). The loan is secured by, among other security documents, two English law debentures made between the Operating Company and the Company, each as chargor, respectively, and Hercules Capital as agent under each agreement. The Hercules Facility terminates on 1 January 2022. The loan bears interest at the rate of the greater of the prime rate as reported in The Wall Street Journal plus 4.50 per cent, and 9.25 per cent. Following any default, a penalty of 5 per cent of the past due amount would be payable on demand and during the period of default the principal, compounded interest and fees would bear an additional interest of 5 per cent, to be compounded into the principal amount outstanding. The Hercules Facility also provided for the US Subsidiary to make customary payments of fees and taxes, such as withholding taxes, if any, on payments made thereunder.

Pursuant to the Hercules Facility, the US Subsidiary had the right to draw down the principal amount of the loan facility in four tranches: (i) $10 million was available on the date of the agreement, (ii) $10 million was to be made available upon approval of BARHEMSYS® by the FDA, but only prior to 30 April 2019, (iii) $5 million was to be made available once the second tranche was drawn, subject to meeting certain additional conditions relating to issuance of additional equity, and (iv) $5 million was available, subject to approval of Hercules Capital's investment committee, upon meeting certain milestone requirements at Hercules Capital's discretion. Drawdowns under the Hercules Facility are subject to customary conditional precedent to closing, including certain warranties and representations and certain certifications of the US Subsidiary and the Company and Operating Company and certain legal opinions of their counsel.

The funds are only for use by the US Subsidiary in refinancing existing indebtedness, paying related fees and expenses, and for working capital and general corporate purposes.

The US Subsidiary secured and drew down the first tranche of $10 million available to it pursuant to the Hercules Facility in June 2018. Because the Group did not achieve approval of the NDA for BARHEMSYS® by 30 April 2019 the second and third tranches of the facility became unavailable. The fourth tranche became unavailable on 1 January 2020.

The Hercules Facility imposes various customary covenants on each of the US Subsidiary, the Company and the Operating Company, including the following, unless otherwise waived:

- to provide financial and other reports to Hercules Capital;
- to provide limited access to certain management records and personnel;
- to refrain from incurring additional indebtedness without Hercules Capital's prior consent, except for pursuant to certain limited exceptions;
- to hold its assets and intellectual property free and clear of encumbrances and liens, without Hercules Capital's prior consent, subject to certain limited customary exceptions;
- to refrain from any investment activities, subject to certain limited customary exceptions;

- to refrain from paying any dividends or making other distributions, or making any loans to employees;
- to refrain from merging or consolidating with any other entity;
- to protect its intellectual property and notify Hercules Capital of any material infringements; and
- to advise Hercules Capital of and pledge as collateral certain material in-licenses.

Warrants over 201,330 Ordinary Shares, exercisable at €3.22 per share, were issued to Hercules Capital pursuant to the Hercules Facility. At the Latest Practicable Date, no warrants had been exercised by Hercules Capital.

The Hercules Facility is governed by the laws of the State of California.

18.12 *Manufacturing Agreements*

The Group relies on a single manufacturer, Patheon UK Limited ("**Patheon**"), for the manufacture of its BARHEMSYS® and BYFAVO™ products, pursuant to manufacturing services agreements for BARHEMSYS® and BYFAVO™, as set out in greater detail below.

(a) BARHEMSYS® Master Manufacturing Services Agreement and Product Agreement

On 8 September 2016, the Operating Company executed a master manufacturing services agreement with Patheon which came into effect from 22 August 2016 (the "**BARHEMSYS® MSA**"). Patheon and the Operating Company entered into a product agreement under the BARHEMSYS® MSA on 20 September 2016 to detail the specific terms relating to the manufacture of APD421 (Amisulpride) Sterile Liquid Vials (CNS 7056) 5mg/mL by Patheon from its manufacturing site in Italy for distribution in the US, including packaging components, minimum volumes and price (the **"BARHEMSYS® Product Agreement**"). Annual volume is expected to increase from 1,875,000 vials in 2019 to 3,200,000 vials in 2020. The BARHEMSYS® Product Agreement does not currently provide for distribution to markets other than the US.

Under the BARHEMSYS® MSA, and in accordance with the specific details set out in the BARHEMSYS® Product Agreement, Patheon agrees to manufacture BARHEMSYS® from active materials provided by the Operating Company. Patheon agrees to perform quality control and quality assurance testing of the product and certify that the products are manufactured in accordance the specifications provided to it by the Operating Company, together with applicable current good manufacturing practices ("**cGMPs**").

The initial term of the BARHEMSYS® MSA will continue until 31 December 2021 before automatically renewing for successive terms of two years each so long as there is a product agreement in effect, unless terminated in accordance with its terms, including if either party gives written notice to the other party of its intention to terminate the agreement at least 18 months prior to the end of the then current term.

Patheon is permitted during the term to make certain price adjustments effective from 1 January of each year for: (i) inflation; (ii) if minimum order quantities or annual volumes are not met; or (iii) for increased component costs, subject to an annual price review and mutual agreement to any adjustments between the parties.

Patheon grants audit, inspection and access rights to its reports and records as well as to areas of the manufacturing site in which BARHEMSYS® is manufactured, stored, handled, or shipped to permit the Operating Company to verify that the manufacturing services are being performed in accordance with its specifications, cGMPs, and applicable laws.

The BARHEMSYS® MSA is governed by English law and subject to the exclusive jurisdiction of the English courts.

(b) BYFAVO™ Manufacturing Services Agreement and Product Agreement

Cosmo is currently party to a manufacturing services agreement with Patheon UK Limited ("**Patheon**") to manufacture BYFAVO™ at Patheon's manufacturing facilities in Italy for distribution in the US (the "**BYFAVO™ MSA**"). Cosmo and Patheon also entered into a product agreement, dated 1 April 2017 (the **"BYFAVO™ Product Agreement**"), which incorporates the terms of the BYFAVO™ MSA and details the specific terms relating to the manufacture of Remimazolam (CNS 7056) 20 mg, including minimum volumes and price. Pursuant to the terms of the BYFAVO™ Wind-Up Agreement, Cosmo and the Group have agreed that Cosmo shall assign the BYFAVO™ MSA and the BYFAVO™ Product Agreement to the Company and the parties are negotiating the terms of such novation with Patheon which may include certain amendments

to the terms of the BYFAVO™ MSA and BYFAVO™ Product Agreement (the "**BYFAVO™ Novation Letter**").

The BYFAVO™ MSA is (and the BYFAVO™ Novation Letter is expected to be) governed by the laws of England and Wales, with any disputes under the BYFAVO™ MSA to be referred for final resolution by arbitration in London under ICC arbitration rules.

18.13 *API Supply Agreements*

The Group currently has entered into one suppy agreement with Icrom for the active pharmaceutical ingredient ("**API**") for each of BARHEMSYS® and APD403, and the FDA has approved a second supplier, Cosma, with whom the Group is negotiating a second supply agreement. The Group expects to receive supply of the API for BYFAVO™ from Paion until the Group is able to reach an alternative supply arrangement.

(a) Icrom API Supply Agreement

On 14 November 2016, the Operating Company entered into a supply agreement with Icrom for the supply of amisulpride API (for both BARHEMSYS® and APD403) for the purpose of manufacturing, marketing and selling pharmaceutical products containing such API (the "**Icrom API Supply Agreement**"). The initial term of the agreement (subject to earlier termination) is seven (7) years, which shall automatically renew for consecutive periods of three (3) years unless either party gives at least one year's notice of non-renewal on expiry of the initial term.

Icrom agrees to manufacture the API, pursuant to purchase orders placed by the Operating Company, in compliance with the Operating Company's specifications, the FDA's current good manufacturing practices and the current "*Drug Master File*" or "*Certificate of suitability of Monographs of the European Pharmacopoeia*" submitted by Icrom to the FDA as well as provide full regulatory support to the Operating Company (in return for a €25,000 regulatory services fee). If by the second anniversary after commercial launch of the applicable product the aggregate annual sales of API by Icrom to the Operating Company are less than €50,000, Icrom is entitled to charge a further annual fee of €20,000.

The agreement is an exclusive supply arrangement under which Icrom shall be (i) the exclusive supplier of API to the Operating Company for the manufacture of products containing the API for four (4) years from the commercial launch date of the applicable product (i.e. BARHEMSYS®) which shall be automatically extended for 1 year unless either party gives at least 6 months' notice of non-renewal; and (ii) the main supplier for the remainder of the term, with a commercial share of at least 66% of the total API volume supplied to the Operating Company in the US or any subsequent territory in which the Operating Company intends to register its pharmaceutical dossier passed on API (the "**Territory**").

In addition to mutual rights of the parties to terminate for the other party's material breach or insolvency event, the Operating Company has the right to terminate the agreement (i) on 60 days' notice if the FDA or any other regulatory authority take any action that would prohibit or materially restrict the manufacture, sale or use of the API in the Territory or (ii) for convenience on at least 6 months' written notice subject to compensation payment to be paid to Icrom of €35,000 per year multiplied by the number of years remaining of the initial term. Icrom has the right to terminate on 60 days' written notice if the Operating Company does not proceed with the applicable product registration, or launch the product in the Territory after regulatory approvals, or otherwise withdraws from the market in the Territory.

The API price is subject to an incremental price reduction in Euros per kg depending on annual volume purchased (e.g. €1,200 per kilo for the first 50kg purchased and €900 if the annual volume purchased is 250kg).

The Icrom API Supply Agreement is governed by English law and subject to the exclusive jurisdiction of the English courts.

(b) Cosmo API Supply Agreement

There is no direct supply agreement yet in place between the Group and a supplier of remimazolam (which is the active ingredient for BYFAVO™). Pursuant to the BYFAVO™ Assignment Agreement, Paion agrees that until a commercial product supply agreement is concluded for the supply of remimazolam by a third party contract manufacturing organisation to the Company, Paion agrees to deliver the API to the Company at cost, which may be via Paion's remimazolam contracted manufacturing organisation.

19. **Properties, Investments, Assets**

The Group's business operates from leasehold premises situated in The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH. The Group currently operates from one UK leasehold property. No single tangible fixed asset (including property, plant and equipment) accounts for more than 10 per cent of the Group's net turnover or production.

On 23 August 2018, Acacia Pharma, Inc. entered into a lease on an office premises in Indianapolis. The lease commences on 1 October 2018 and has a term of 5 years and 2 months. The annual rent cost is $0.1 million.

20. **Disclosures under the Market Abuse Regulation**

The table below sets out a summary of the information disclosed by the Company under the Market Abuse Regulation over the last 12 months:

Date	Title of Announcement	Disclosure
13 August 2020	Interim Results for the Six Months ended 30 June 2020	The Company announces its unaudited interim results for the six-month period ended 30 June 2020
27 July 2020	Second API Supplier for BARHEMSYS® Receives FDA Approval	The Company announces that the FDA has approved a second supplier for the active pharmaceutical ingredient (API) for BARHEMSYS® (amisulpride injection)
16 July 2020	Issue of Equity pursuant to Sub-Licensing Agreement with Cosmo	The Company issued 4,923,811 Shares to Cosmo pursuant to the BYFAVO™ sub-licensing agreement following FDA approval of BYFAVO™
15 July 2020	Acacia Pharma Assigned US License for BYFAVO™ (remimazolam) by Cosmo	The Company has been assigned the US license to BYFAVO™ (remimazolam) for injection by Cosmo. The terms of the license agreement that Acacia Pharma entered into in January 2020 remain unchanged but will now be between Acacia Pharma and Paion. Cosmo will no longer be a party to that agreement
2 July 2020	Acacia Pharma announces US FDA Approval of BYFAVO™ (remimazolam) for injection for the induction and maintenance of procedural sedation	The US Food and Drug Administration (FDA) has approved BYFAVO™ (remimazolam) for injection for the induction and maintenance of procedural sedation
1 June 2020	Debt for Equity Swap with Cosmo Pharmaceuticals	Acacia Pharma issued Ordinary Shares in connection with the termination of a loan agreement with Cosmo
8 May 2020	Issue of equity on exercise of option/vesting of performance share awards	The Company issued 14,391 Ordinary Shares to satisfy options granted under the Company's Enterprise Management Incentive Share Option Plan
7 May 2020	Issue of equity on exercise of option/vesting of performance share awards	The Company issued 140,000 Ordinary Shares to satisfy options granted under the Company's Enterprise Management Incentive Share Option Plan
7 April 2020	Appointment of Director	Acacia Pharma announces the appointment of Alessandro Della Chà as a non-executive director of the Company
24 March 2020	Publication of Prospectus	Acacia Pharma announces the publication of a prospectus in relation to future issues of Ordinary Shares to Cosmo

Date	Title of Announcement	Disclosure
12 March 2020	Acacia Pharma Announces Brief Extension of FDA Review Period for NDA for BYFAVO™	Acacia Pharma announces the FDA has set a new Prescription Drug User Fee Act (PDUFA) goal of reviewing and acting on the NDA for BYFAVO™ of no later than 5 July 2020 (previous PDUFA target date was 5 April 2020)
2 March 2020	Changes to officers and Board of Directors	Acacia Pharma announces changes to its officers and Board of Directors
2 March 2020	Annual Report	Acacia Pharma Group plc: Results for the year ended 31 December 2019
27 February 2020	Acacia Pharma announces US FDA Approval of BARHEMSYS® (amisulpride) for the Treatment and Prevention of Postoperative Nausea and Vomiting (PONV)	The US Food and Drug Administration (FDA) has approved BARHEMSYS® (amisulpride injection) for the prevention of PONV in adult patients
13 January 2020	Acacia Pharma Group plc announces planned CFO succession	Christine Soden to step down and Gary G. Gemignani to be appointed new CFO
10 January 2020	Acacia Pharma enters into strategic in-licensing, investment and loan transaction with Cosmo	• Acacia Pharma has in-licensed exclusive rights to ultra-short-acting sedative BYFAVO™ (remimazolam) from Cosmo • Cosmo will make a €10 million equity investment in Acacia Pharma and provide a new €35 million loan facility to support commercial activities
26 September 2019	Acacia Pharma Announces New BARHEMSYS® PDUFA Target Date of 26 February 2020	The FDA accepted the Company's resubmitted NDA for BARHEMSYS® (amisulpride injection), classified the resubmission as Class 2 and gave a PDUFA goal of reviewing and acting on it no later than 26 February 2020

21. Expenses of the Fundraising and Admission

The total costs and expenses of, and incidental to, the Fundraising and Admission (including the admission fees, advisers' fees, professional fees and expenses and VAT thereon, if any) to be borne by the Company are estimated to be approximately €2.9 million.

22. Auditors

PricewaterhouseCoopers LLP ("**PwC**"), whose registered office is situated at 1 Embankment Place, London WC2N 6RH and whose address is The Maurice Wilkes Building, St John's Innovation Park, Cowley Road, Cambridge CB4 0DS, UK, have been the independent auditors of the Company since its incorporation in 2015 and of the Operating Company since 2007. PwC is a member of the Institute of Chartered Accountants in England and Wales.

23. Documents available for inspection

Copies of the following documents may be inspected at the registered office of the Company at The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH, during normal business hours on any weekday (Saturdays, Sundays and public holidays excepted) for a period of 12 months from the date of publication of this Prospectus:

- the Articles; and
- the documents incorporated by reference into this Prospectus as described in Part XI (*Historical Financial Information*).

For the purposes of PR 3.2.2 of the Prospectus Regulation Rules, the Prospectus will also be published in printed form and available free of charge, during normal business hours on any weekday (Saturdays, Sundays and public holidays excepted) for a period of 12 months from the date of publication of this Prospectus at the registered office of the Company at The Officers' Mess, Royston Road, Duxford, Cambridge CB22 4QH. In addition, the Prospectus will be published in electronic form and be available on the Company's website at www.acaciapharma.com, subject to certain access restrictions.

PART XV

DEFINITIONS

The following definitions apply throughout this Prospectus unless the context requires otherwise:

€10 million Loan Agreement	the agreement dated 10 January 2020 entered into between the Operating Company and Cosmo as described in Section 18.6 of Part XIV of this document (*Additional Information*);
€25 million Loan Agreement	the agreement dated 10 January 2020 as amended on 22 July 2020 entered into between the Company, the Operating Company, the US Subsidiary and Cosmo as described in Section 18.6 of Part XIV of this document (*Additional Information*);
2015 Plan	the Acacia Pharma Group plc 2015 Discretionary Share Option Plan;
2018 Annual Financial Statements	the audited consolidated financial statements for the Company for the 12 months ended 31 December 2018;
2019 Annual Financial Statements	the audited consolidated financial statements for the Company for the 12 months ended 31 December 2019;
2020 Interim Financial Statements	the unaudited consolidated financial statements for the Company for the six months ended 30 June 2020;
Admission	admission of the New Ordinary Shares to trading on the regulated market of Euronext Brussels;
Articles	the articles of association of the Company;
ASCO	American Society of Clinical Oncology;
Audit Committee	the audit committee of the Board or a sub-committee of it;
Banks or Joint Bookrunners	Jefferies, Guggenheim Securities and the Listing Agent;
BARHEMSYS® MSA	the master manufacturing services agreement dated 22 August 2016 entered into between Patheon and the Operating Company, as described in Section 18.12 of Part XIV of this document (*Additional Information*);
BARHEMSYS® Product Agreement	the agreement dated 20 September 2016 entered into between Patheon and the Operating Company, as described in Section 18.12 of Part XIV of this document (*Additional Information*);
Belgian FSMA	the Belgian Financial Services and Markets Authority;
BYFAVO™ Acquisition	the acquisition of the licensing rights in the US to BYFAVO™ as described in the BYFAVO™ Assignment Agreement and BYFAVO™ Wind-Up Agreement;
BYFAVO™ Approval	approval by the FDA of the new drug application filed with number 212295 for BYFAVO™ (Remimazolam) in the indication of procedural sedation, received on 2 July 2020;
BYFAVO™ Assignment Agreement	the agreement dated 13 July 2020 entered into between the Operating Company, Paion and Cosmo, as described in Section 18.4 of Part XIV of this document (*Additional Information*);
BYFAVO™ First Commercial Sale	the first commercial sale of BYFAVO™ in the United States;
BYFAVO™ Head-Licence Agreement	the agreement to commercialise and develop BYFAVO™ in the United States entered into on 24 June 2016 between Cosmo and Paion, as described in Section 18.3 of Part XIV of this document (*Additional Information*);
BYFAVO™ MSA	the master manufacturing services agreement dated 1 April 2017 entered into between Patheon and Cosmo, as described in Section 18.12 of Part XIV of this document (*Additional Information*);

BYFAVO™ Novation Letter	an agreement proposed to be entered into between the Group, Cosmo and Patheon to assign to the Group the BYFAVO™ MSA and BYFAVO™ Product Agreement as described in Section 18.12 of Part XIV of this document (*Additional Information*);
BYFAVO™ Product Agreement	the existing agreement entered into between Cosmo and Patheon, which is proposed to be assigned to the Company as described in Section 18.12 of Part XIV of this document (*Additional Information*);
BYFAVO™ Sub-Licence Agreement	the agreement dated 10 January 2020 entered into between the Operating Company, the Company and Cosmo, which has now been terminated, as described in Section 18.3 of Part XIV of this document (*Additional Information*);
BYFAVO™ Wind-Up Agreement	the agreement dated 15 July 2020 entered into between the Operating Company, the Company and Cosmo, as described in Section 18.4 of Part XIV of this document (*Additional Information*);
certificated or in certificated form	shares or other securities recorded on the relevant register as being held in certificated form;
City Code	the UK City Code on Takeovers and Mergers;
Companies Act	the UK Companies Act 2006, as amended;
Company or Acacia Pharma	Acacia Pharma Group plc, registered in England and Wales with company number 09759376;
Cosmo	Cosmo Technologies Limited, a wholly-owned subsidiary of Cosmo Pharmaceuticals N.V.;
Cosmo Guarantees	the guarantees dated 10 January 2020 entered into between the Company, the US Subsidiary and Cosmo as described in Section 18.7 of Part XIV of this document (*Additional Information*);
Cosmo Loan Agreements	the loan agreements dated 10 January 2020, as amended, entered into between the Operating Company and Cosmo as described in Section 18.6 of Part XIV of this document (*Additional Information*);
CSOP	Company Share Option Plan;
DABP	Deferred Annual Bonus Plan;
Deed of Termination and Release	the deed of termination and release dated 30 May 2020 entered into between the Company, the Operating Company, the US Subsidiary and Cosmo as described in Section 18.10 of Part XIV of this document (*Additional Information*);
Directors or Board	the Executive Directors and the Non-Executive Directors;
Disclosure Guidance and Transparency Rules	the disclosure guidance and transparency rules made by the FCA under Part VI of FSMA;
EAPO	Eurasian Patent Office;
EMI Plan	the Acacia Pharma Group plc 2015 Enterprise Management Incentive Plan;
EPO	European Patent Office;
ESMO	European Society for Medical Oncology;
European Community	all European Union Member States;
European Economic Area or EEA	the European Union, Iceland, Norway and Liechtenstein;
European Union or EU	an economic and political union of Member States which are located primarily in Europe;
Executive Director	the executive director of the Company, being Michael Bolinder;

Executive Management Team	the Group's executive management team comprising Michael Bolinder, Gary Gemignani and Dr Gabriel Fox;
Executive Share Plans	the PSP, the DABP and the CSOP;
Existing Ordinary Shares	the 72,779,729 existing Ordinary Shares of £0.02 each in nominal value in the capital of the Company at the date of this Prospectus;
Existing Shareholders	holders of Existing Ordinary Shares immediately prior to Admission;
FCA	the UK Financial Conduct Authority;
FDA	the US Food and Drug Administration;
FINRA	the US Financial Industry Regulatory Authority, Inc.;
First Cosmo Investment Agreement	the investment agreement dated 10 January 2020 entered into between Cosmo and the Company as described in Section 18.6 of Part XIV of this document (*Additional Information)*;
F-Prime	F-Prime Capital Partners Healthcare Fund III LP;
FSMA	the UK Financial Services and Markets Act 2000 (as amended);
FTT	the European Commission's proposed Directive of a common Financial Transaction Tax;
Fundraising	the issue of New Ordinary Shares described in this Prospectus;
Gilde	funds advised by Gilde Healthcare Partners B.V.;
Group	Acacia Pharma Group plc and its subsidiary undertakings taken as a whole;
Guggenheim Securities	Guggenheim Securities, LLC;
Hercules Capital or Hercules	Hercules Capital Inc.;
Hercules Facility	the facility provided by Hercules Capital pursuant to an agreement dated 29 June 2018 between the Company, the US Subsidiary and Hercules Capital as described in Section 18.11 of Part XIV of this document (*Additional Information*);
HMRC	HM Revenue and Customs in the UK;
Icrom	Icrom SpA;
IFRS	International Financial Reporting Standards, as adopted by the European Commission for use in the European Union;
IGA	intergovernmental agreements;
Initial Consideration	the initial consideration payable under the BYFAVO™ Sub-licence Agreement as described in Section 18.3 of Part XIV of this document (*Additional Information*);
IPO	the initial global offer of Ordinary Shares to certain institutional and professional investors made by way of a prospectus relating to the Company dated 2 March 2018 and admission of the Ordinary Shares to trading on the regulated market of Euronext Brussels (which became effective on 6 March 2018);
ISIN	International Securities Identification Number;
Jefferies	Jefferies International Limited;
Latest Practicable Date	close of business on 12 August 2020;
LEI	Legal Entity Identifier;
LIBOR	London inter-bank offered rate;

Listing Agent	Bank Degroof Petercam SA/NV, having its registered office at Nijverheidsstraat 44, 1040 Brussels, Belgium;
Loan Parties	has the meaning set out in Section 18.8 of Part XIV of this document (*Additional Information*);
Lock-up Agreements	the lock-up deeds entered into by each of the Directors, the Senior Managers and Cosmo in favour of the Banks described in Section 18.2 of Part XIV of this document (*Additional Information*);
Lundbeckfond	Lundbeckfond Invest A/S;
Member State	a member state of the European Union;
New Ordinary Shares	those Ordinary Shares to be issued by the Company pursuant to the Fundraising;
Nomination Committee	the nomination committee of the Board or a sub-committee of it;
Non-Executive Directors	the non-executive directors of the Company, being Scott Byrd, Dr John Brown, Edward Borkowski and Alessandro Della Chà;
Novo	Novo Holdings A/S;
Operating Company	Acacia Pharma Limited, registered in England and Wales with company number 05934843;
Ordinary Shares or Shares	ordinary shares of £0.02 each in the capital of the Company;
Paion	Paion UK Limited, a wholly-owned subsidiary of Paion AG;
Patheon	Patheon UK Limited;
PCAOB Standards	the Public Company Accounting Oversight Board Standards;
PCT	Patent Co-operation Treaty;
PDUFA	the US Prescription Drug Fee User Act;
Placing Price	€2.00 per New Ordinary Share;
Prospectus	this document;
Prospectus Regulation or PR Regulation	Prospectus Regulation (2017/1129/EC);
Prospectus Regulation Rules	the Prospectus Regulation Rules of the FCA made under Part VI of FSMA relating to offers of securities to the public and admission of securities to trading on a regulated market;
PSP	Performance Share Plan;
Qualified Institutional Buyer or QIB	a qualified institutional buyer within the meaning of Rule 144A;
Registrar	Equiniti Limited;
Regulation S	Regulation S under the Securities Act;
Remuneration Committee	the remuneration committee of the Board or a sub-committee of it;
Revenue Code	the US Internal Revenue Code of 1986, as amended;
RIS	a regulatory information service authorised by the FCA to release regulatory announcements to the London Stock Exchange;
Rule 144A	Rule 144A under the Securities Act;
SDRT	UK stamp duty reserve tax;
Securities Act or US Securities Act	the US Securities Act of 1933, as amended;
Second Cosmo Investment Agreement	the investment agreement dated 30 May 2020 entered into between Cosmo and the Company as described in Section 18.9 of Part XIV of this document (*Additional Information)*;

Senior Managers	those persons identified as Senior Managers of the Group in Part VII of this document (*Directors, Senior Managers and Corporate Governance*);
Share for Share Exchange	the share for share exchange transaction by which the Company acquired all the issued shares in the capital of the Operating Company, referred to in Section 7 of Part XIV of this document (*Additional Information*);
Shareholder(s)	holder(s) of shares in the capital of the Company from time to time;
SID	senior independent director of the Board;
Subordination Agreement	the agreement dated 10 January 2020 entered into between the Company, the US Subsidiary, the Operating Company, Hercules Capital and Cosmo described in Section 18.8 of Part XIV of this document (*Additional Information*);
Takeover Directive	The European Directive on Takeover Bids (2004/25/EC);
Takeover Panel or Panel	the UK Panel on Takeovers and Mergers;
TSR	total shareholder return;
UK or United Kingdom	the United Kingdom of Great Britain and Northern Ireland;
UK Corporate Governance Code	the UK Corporate Governance Code issued by the Financial Reporting Council as amended from time to time;
uncertificated or in uncertificated form	shares or other securities recorded on the relevant register as being held in uncertificated form in Euroclear Belgium and title to which, by virtue of the rules and procedures of Euroclear Belgium, may be transferred by means of Euroclear Belgium;
US GAAP	US Generally Accepted Accounting Principles;
US GAAS	US Generally Accepted Auditing Standards; and
US Subsidiary	Acacia Pharma, Inc., registered in Delaware with number 5799660.

PART XVI

GLOSSARY

The following explanations are not intended as technical definitions, but rather are intended to assist the reader in understanding certain terms used in this Prospectus:

adverse event	any untoward medical occurrence in a subject in a clinical trial who has been administered a pharmacological product whether or not it has a causal relationship with the product;
agent	an active force or substance capable of producing an effect;
agonist	a compound which binds to a receptor on or in a cell and which, as a consequence, evokes an active response;
ANDA	Abbreviated New Drug Application;
antagonist	a compound which binds to a receptor on or in a cell and which, as a consequence, prevents the usual response or activity of that receptor;
antiemetic	a substance which prevents or suppresses vomiting and/or nausea;
antipsychotic	a drug which prevents or supresses manifestations of psychotic disorders, such as schizophrenia and mania;
API	active pharmaceutical ingredient;
ASP	average selling price;
boxed warning –	the strictest warning put in the labelling of prescription drugs or drug products by the FDA when there is reasonable evidence of an association of a serious hazard with the drug (also known as a black-box warning);
broad label	a marketing approval for a drug with relatively few restrictions in how that drug may be used in its therapeutic area;
CAPA Plan	corrective and preventative action plan;
chemotherapy	the treatment of disease by means of chemicals that have a specific toxic effect upon agents of the disease, such as cancer cells or pathogenic micro-organisms;
chronic	characterised by extended duration and typically by slow development or slow recurrence of a disease, as opposed to acute;
CINV	chemotherapy induced nausea and vomiting;
Consensus Guidelines	guidelines for managing post-operative nausea and vomiting, published by Gan TJ, Belani KG, Bergese SD, et al (2020), "Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting" *Anesth Analg,* doi: 10.1213/ANE.0000000000004833;
CRL	complete response letter;
CRO	contract research organisation;
data exclusivity	the exclusive right of an applicant over the regulatory data it submits to obtain marketing authorisation for a medicinal product. During a period of data exclusivity, other applicants (such as generic drug manufacturers) seeking to obtain marketing authorisation are prevented from referring to or otherwise making use of such data in their own applications;
double-blind	a kind of clinical study comparing two or more treatments, in which the identity of each individual treatment is concealed from the study subjects and the researchers. This method minimises the bias, deliberate or unintentional, which may arise if the treatment for a particular subject is known;

emetogenic	inducing nausea and/or vomiting, a common property of anti-cancer agents and opioid pain killers, among other drugs;
enantiomers	chiral molecules that are mirror images of one another;
endpoint	in a clinical trial, a measure chosen for statistical testing to determine whether an experimental treatment is or is not different from a reference treatment. The primary endpoint is the most important measure in the trial and is used to calculate the required number of subjects;
extrapyramidal side effects (EPS)	signs and symptoms arising from the blockage of pathways in the brain involved in the coordination of movement, including restlessness, twitches, muscle spasms, rigidity and irregular, jerky movements;
extravasation	a discharge or escape, as of blood, from a vessel into the tissues;
FDA	the Food and Drug Administration of the US, responsible as 'public health protector' for overseeing the approval process for a new drug or device to be marketed;
formulary	a hospital's list of approved products;
formulation	the combination of active drug and pharmacologically inactive ingredients used to achieve adequate bioavailability;
GCP	Good Clinical Practice;
GMP	Good Manufacturing Practice;
HEC	highly emetogenic chemotherapy, an anti-cancer drug or regimen which causes nausea and vomiting in more than 90 per cent of recipients, in the absence of effective prevention;
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use;
ICU	intensive care unit;
indication	a particular therapeutic use of a drug;
initial label	the approved use(s) of a drug on its first introduction into the market;
intravenous or IV	with a vein;
label	the terms of a drug's marketing approval, in particular the therapeutic areas and patient populations in which it is approved to be used;
Late Stage	in Phase 2 clinical development or later;
KOL	key opinion leader;
MA	market authorisation;
MEC	moderately emetogenic chemotherapy regimens that are linked to a moderate incidence of nausea and vomiting;
Medicaid	a US joint federal-state programme that provides health coverage or nursing home coverage to certain categories of low-asset people, including children, pregnant women, parents of eligible children, people with disabilities and elderly needing nursing home care;
Medical Science Liaisons	healthcare professionals employed by pharmaceutical companies within their medical teams as a communication bridge with clinical medicine, acting as the company's spokesperson and educator;
Medicare	the US federal health insurance programme for people who are 65 or older, certain younger people with disabilities, and people with End-Stage Renal Disease;
NDA	New Drug Application;

NK-1 receptor antagonist	a substance which antagonises neurokinin-1 receptors, these have been shown to have antidepressant aniolytic and antiemetic properties;
off-label use	use of a drug for a disease or condition other than the indication for which it was approved;
OINV	opioid-induced nausea and vomiting;
oncologist	a specialist physician who treats cancer patients;
open-label	a kind of study where the identity of treatments is not concealed;
P&T committee	pharmacy and therapeutics committee;
PARP	poly-ADP ribose polymerase;
pharmacological	relating to the study of drugs, especially in respect of their effects on body systems, such as tissues, cells, receptors, etc.;
Phase 2	an exploratory stage of clinical testing, in which the aim is usually to obtain initial evidence of efficacy and safety in target patients and to characterise the relationship between dose and response;
Phase 2a or Phase 2/3	a kind of study with features of both Phase 2 and Phase 3 trials, usually applied to a trial which is designed to start with multiple treatment arms and undergo one or more analyses during its course with a view to discontinuing less effective treatment arms, leading to a final comparison of the optimal treatment arm with the reference arm;
Phase 3 or Phase 3	the final stage of clinical testing prior to drug approval, in which the aim is to obtain statistically persuasive evidence of efficacy and substantial evidence of adequate safety in one or more target patient populations;
PONV	post-operative nausea and vomiting;
PONV Consensus Guidelines	the 2014 Consensus Guidelines for managing Post-Operative Nausea and Vomiting;
prevalence	the number of individuals in a population having a particular condition at a particular point in time;
prodrug	a substance which is itself not an active drug but which is, after administration, converted into an active drug by the body;
prophylactic antiemetic	an antiemetic given to prevent the onset of nausea and/or vomiting;
prophylaxis	treatment given or action taken to prevent a disease or condition;
QT interval	the time between the start of the Q wave and the end of the T wave on an electrocardiogram, representing the time taken for depolarisation (electrical discharge) and repolarisation of the heart ventricles during each heart beat;
QTc	the QT interval mathematically adjusted to take account of the heart rate;
radiotherapy	the treatment of disease, usually cancer, using ionising radiation;
randomised	a kind of study in which participants are allocated to treatment groups at random;
regimen	a specific combination or sequence of drugs for preventing or treating a disease or condition;
relative risk reduction	the amount by which a treatment reduces the chance of an undesirable outcome compared to a reference, such as a placebo or a current standard, expressed as a percentage of the reference effect; for example, a treatment which reduced an outcome from 50 to 40 per cent would

	give a relative risk reduction of 10 divided by 50, or 20 per cent. This is effectively a measure of the proportion of patients benefitting from the treatment;
Type B meeting	pre-investigational NDA meetings, certain end-of-Phase 1 meetings, end-of-Phase 2 and pre-Phase 3 meetings and pre-new drug application/ biologics licence application meetings with the FDA; and
WAC	wholesale acquisition cost